

A STUDY OF THE DISTRIBUTION OF PHOSPHORUS AND  
CALCIUM IN BLOOD OF CHILDREN IN  
HEALTH AND DISEASE.

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the University of Edinburgh.

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P R E F A C E.

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Lastly/

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## P A R T I.

### Introduction.

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During the past 15-20 years our knowledge concerning the phosphorus content of the blood has been considerably advanced by the work of several investigators. The inorganic phosphorus fraction, which is only about  $1/10$  of the total phosphorus compounds of the whole blood, appears to have claimed the attention of most of the previous workers, and, therefore, abundant data are available from the literature both for health and disease. Because of this, the inorganic phosphorus fraction of the blood has already acquired some definitely practical clinical value.

The other fractions of the phosphorus of the blood have attracted the attention of fewer workers, and have been less studied with the obvious result that such scanty observations as are available, are still of only theoretical interest and no clinical value.

In view of this scanty information as to the total content and the distribution of the phosphorus compounds in the blood it seemed advisable further to investigate the question and the present communication is an attempt to do this using the child chiefly as the material.

Distribution of Different Forms of Phosphorus in Blood.

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A great deal of the earlier work on the phosphorus compounds in human blood is invalidated, because no suitable precautions were taken to prevent hydrolysis of various moieties of the phosphorus.

(1)  
Martland, Hansman and Robison (1924) and Lawaczek  
(2)  
(1924) have shown conclusively that, if the blood has been laked, a rapid increase in the amount of the inorganic phosphorus fraction of the blood occurs even at room temperature. This increase in the inorganic phosphorus fraction is due to the hydrolysis of phosphoric esters by the enzymes liberated from the laked corpuscles. Further-  
(3)  
more, Kay and Byron (1927) have pointed out that even after the precipitation of the proteins, blood filtrates, if allowed to stand in acid solutions for any length of time, undergo a slow hydrolysis of their organic phosphorus compounds.

Unlaked blood which is not allowed to become alkaline owing to the loss of carbon dioxide may be kept for several minutes at room temperature before any detectable change in its inorganic phosphorus fraction takes place. If the blood becomes more alkaline the inorganic phosphorus diminishes at first, and then, slowly rises again. If the blood is made slightly acid the inorganic phosphorus fraction rises from the beginning. Owing to the loss of carbon/

carbon dioxide on defibrination, with the resulting alkalinity and synthesis of the inorganic phosphorus into an organic form, the serum may contain a smaller inorganic phosphorus fraction than the plasma. On the strength of these findings it is essential to follow most scrupulously the technique laid down so that the quantitative value of the "inorganic" and so-called "organic acid soluble" phosphorus of the blood be relatively correct.

(4)

Bloor published, some 12 years ago, his important work on the phosphorus compounds of the human blood. For the sake of convenience he divided phosphoric acid compounds into two different groups:-

(a) The acid soluble - soluble in dilute acids and precipitated with the proteins by the alcohol-ether solution.

(b) The lipoid phosphoric acid compounds - soluble in alcohol-ether solution, and precipitated with the proteins by dilute acids.

Bloor showed that these two groups are apparently sharply defined, and, since in general, their sum total is equal to the total phosphorus of the blood the presence of other forms of the phosphoric combinations in blood in significant amounts is doubtful.

The acid soluble fraction comprises the small amount of inorganic phosphorus and a very much larger fraction of the organic phosphorus. Bloor (1918) and Zucker and Gutman (1923) showed, however, that the phosphorus in the organic/

organic combinations can be liberated by hydrolysis with acids, and Kay and Robison (1924)<sup>(6)</sup>, and Kay (1926)<sup>(7)</sup> pointed out that this liberation can be brought about by the enzymes as well.

The lipoid phosphoric acid compounds comprise lecithin, kephalin, and sphingomyelin. Bloor (1916)<sup>(8)</sup> studied "fats" in the normal human blood, and he found that the lecithin (lipin) content of the corpuscles of the blood is approximately double that of the plasma. De Wesselow (1924)<sup>(9)</sup> confirmed this.

There is also a relatively minute quantity of nucleic acid present in leucocytes which does not appear in either group (a) or (b).

Further, phosphorus in organic combination is also present in the specimens of serum albumin and globulin which have not been extracted with the alcohol-ether solution, but, according to Sørensen (1926)<sup>(10)</sup>, this organic phosphorus is not an integral portion of the protein molecule, since the alcohol-ether extraction at  $-4^{\circ}$  removes it almost completely. He believed that both these proteins, when pure, would be found to be phosphorus-free.

Up till 1923 there were only two organically bound phosphorus compounds known, namely, nucleoprotein and lipin phosphorus, but Jackson (1923 and 1924)<sup>(11)</sup><sup>(12)</sup> isolated and identified a third compound as adenine nucleotide. Kay and Robison (1924)<sup>(6)</sup> showed that there were, at least, two classes of

of the acid soluble organic phosphorus in blood, some 25-35 per cent of the acid soluble phosphorus being hydrolysed rapidly at 38° by means of an enzyme which could be extracted from bone, whilst the remainder of the organic phosphorus was not hydrolysed by this agent.

(13)  
Goodwin and Robison (1924) separated a reducing phosphoric ester, and Greenwald (1925) isolated a compound without reducing properties which he has shown to be a salt of the diphosphoric ester of 1-glyceric acid.

(3)  
Kay and Byrom (1927) classified phosphorus compounds of the blood in the following manner:-

- |   |   |                       |   |                                 |
|---|---|-----------------------|---|---------------------------------|
| 1. Inorganic phosphate.   | } | "Ester<br>Phosphorus" | } | "Acid<br>Soluble<br>Phosphorus" |
| 2. Nucleotide phosphate.  |   |                       |   |                                 |
| 3. Phosphoglyceric acid.  |   |                       |   |                                 |
| 4. Reducing phosphoric ester.   |   |                       |   |                                 |
| 5. At least one other phosphoric ester.                               |   |                       |   |                                 |
| 6. Lecithin.  | } |                       |   |                                 |
| 7. Kephalin.  |   |                       |   |                                 |
| 8. Sphingomyelin.   |   |                       |   |                                 |
| 9. Nucleic acid (residual phosphorus (very small in total quantity)). |   |                       |   |                                 |

#### Composition of Human Blood.

Blood is composed of (1) plasma, (2) red blood corpuscles, (3) white blood cells, and (4) platelets. These four elements of the blood contain unequal amounts of different phosphorus compounds. (15)  
Kay (1926) showed that the white blood cells (leucocytes) and the platelets are richer in the/



the phosphorus compounds than the red blood corpuscles, but unless they were abnormally high in number in a given specimen of blood their fraction of the phosphorus compounds could be neglected. In the abnormal blood, however, they must be checked by the process of counting or by means of the haematocrit.

Practically all, but not quite all, the ester phosphorus of the blood is present in the red blood corpuscles. Martland and Robison (1926)<sup>(16)</sup> and Kay (1926)<sup>(7)</sup> showed that about 1 per cent of the total ester phosphorus in 100 c.c. of whole blood is present in the plasma, and that it is hydrolysed by tissue phosphatases. About 2 per cent of the ester phosphorus is present in the white blood cells and platelets, and the rest (97%) is present in the red blood corpuscles.

#### Survey of the Literature on the Phosphorus Compounds of Normal Blood.

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The most important part of the work on the phosphorus compounds of the human blood has been carried out during the last twenty years.

As the literature is fairly extensive it is thought more convenient to collect and present in a tabulated form the various findings of most of the previous workers regarding the phosphorus compounds of the human blood in normal/



normal subjects. These results will be found in Tables I and II.

It is of interest, however, to mention specially the important work of Meigs, Blatherwick, and Carey (1919)<sup>(32)</sup> who examined 47 samples of animals' plasma for the lipid, inorganic, and total phosphorus. They found that the sum total of the lipid and inorganic phosphorus fraction is generally a little lower than the total determined independently, the difference amounting, on the average, to 0.26 mg. per 100 c.c. of plasma. They concluded that the plasma of normal blood contains no phosphorized proteins, and probably no phosphorus compounds at all except phosphatides, and inorganic phosphates. Both of these undergo variations with increasing age and during pregnancy. The phosphatides of the plasma show a marked tendency to rise during the first month of lactation and to remain high until lactation ceases. De Wesselow (1922)<sup>(33)</sup> similarly found in women that the inorganic phosphates fell towards the end of pregnancy, and rose during the period of lactation.

Hess and Lundagen (1922)<sup>(34)</sup> examined the blood of infants at different times of the year, and they showed that there is a seasonal tide in the inorganic phosphates in children. They found 3.92 mg. of the inorganic phosphate in 100 c.c. of blood in December whereas in summer 4.34 mg. per 100 c.c. of blood. The tide appeared to be the lowest in March, and in April began to rise, ascending markedly in May and rising/

Table I.

Author's Name.	Plasma.		Serum.	Whole Blood.	
	Inorganic Phosphorus. mgm./100c.c.	Inorganic Phosphorus. mgm./100c.c.		Inorganic Phosphorus. mgm./100c.c.	Inorganic Phosphorus. mgm./100c.c.
Marriott & Howland (1916) (23) 1. Average (37) normal adults.	-	-	1.0 - 3.5	-	-
Denis & Minot (1921) (24) 2. Average for normal adults.	1.2 - 3.1	-	-	-	-
Howland & Kramer (1921) (25) 3. Average for normal children.	-	5.4	-	-	-
Hess & Gutman (1922) (26) 4. Average for normal children.	-	-	-	4.0	-
Von Meysenburg (1922) (27) 5. Average for normal children.	-	5.0	-	-	-
Zucker & Gutman (1923) (28) 6. Average for normal children.	-	-	-	4.6	-
Tolstoi (1923) (29) 7. Average for normal adults.	2.5 - 3.3	2.5 - 3.3	-	-	-
Anderson (1924) (30) 8. Average for normal children.	-	-	-	4.8	-
Riesenfeld, Rose, & Handelsman (1925) (31) 9. Average for mothers. Average for infants.	-	-	-	3.1 4.12	-

Table II.

Author's Name.	Plasma or Serum					Whole Blood				Corpuscles.				Haema- tocrit	Organ. Phosph. Index.	Remarks.
	I.P.	E.P.	L.P.	T.P.	A.S.P.	T.P.	L.P.	I.P.	E.P.	T.P.	L.P.	I.P.	E.P.			
	mgm. per 100			c.c.			mgm. per 100 c.c.			mgm. per 100 c.c.						
Taylor & Miller 1. (1914) <sup>19</sup>	0	0		4-6	-	-	-	-	-	-	-	-	-	-	-	Serum.
Greenwald (1915) <sup>17</sup> 2. Average (12 N. adults)	-	-	9.8	13.9	4.3	-	-	-	-	-	-	-	-	-	-	Serum.
Jones & Nye (1921) <sup>18</sup> 3. Average for children.	2.9	0	9.3	12.0	-	38.0	13.0	3.1	22.0	80.0	19.0	3.46	57.6			Calculation Plasma.
McKellips, De Young, & Bloor (1921) <sup>20</sup> 4. Average for children.	3.1	2.0	4.5	9.2	5.0	-	-	-	-	75.7	17.0	4.59	49.6	44.3	-	Calculation Plasma.
Bloor (1918) <sup>21</sup> 5. Average for N. adults	3.05	0.46	7.15	10.65	3.6	-	-	-	-	77.8	18.7	5.3	52.9	-	-	Plasma.
Kay & Byrom (1927) <sup>3</sup> 6. Average for N. adults.	-	-	7.1	-	-	37.8	12.0	3.1	22.7	-	18.	-	-	43.	53	Plasma.
Harrison (1930) <sup>22</sup> 7. Average for adults	1-5	0-4	3-13	6-15	2-8	28-48	8-16	2-6	14-29							Plasma.
Stamford & Wheat- ley (1925) <sup>40</sup> 8. Average (5)	2.9	0.32	6.8	10.0	-	36.8	10.7	3.0	23.1	63.6	13.1	2.16	48.4	46.3	-	Plasma.

I.P.= Inorganic Phosphorus; E.P.= Ester Phosphorus; L.P.= Lipin Phosphorus; T.P.= Total Phosphorus; A.S.P.= Acid soluble phosphorus

P A R T 2.Author's Results.

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Method:

The method used for all the estimations of the phosphorus compounds of the human blood in this work was that adopted and described fully by Kay and Byrom (1927)<sup>(3)</sup> with one or two slight modifications that were found inevitable in the process of its application. This method however, actually consists of Brigg's (1922)<sup>(35)</sup> modification of Bell and Doisy's (1920)<sup>(36)</sup> colorimetric method for the estimation of inorganic and ester phosphorus and Randles and Knudson's (1922)<sup>(37)</sup> method for the estimation of the lipin phosphorus content of the blood.

Owing to the technical difficulties it was decided to omit the estimations of the hydrolysable and non-hydrolysable ester phosphorus fractions in this work.

For the purpose of complete analysis about 20 c.c. of the oxalated human blood were used, and the following independent estimations were done on each specimen of blood:-

1. Haematocrit value.
2. Inorganic or free phosphates of the whole blood.
3. Inorganic plus ester phosphorus of the whole blood.
4. Lipin phosphorus of the whole blood.
5. Total phosphorus of the whole blood.



6. Inorganic phosphate of the plasma.
7. Inorganic and ester phosphorus of the plasma.
8. Lipin phosphorus of the plasma.
9. Total phosphorus of the plasma.

From the findings of the above enumerated estimations the following were calculated:-

- x 1. Total phosphorus of the whole blood.
- 2. Ester phosphorus of the whole blood.
- 3. Ester phosphorus of the plasma.
- x 4. Total phosphorus of the plasma.
5. Inorganic or free phosphate of the red blood corpuscles.
- 6. Ester phosphorus of the red blood corpuscles.
7. Lipin phosphorus of the red blood corpuscles.
- x 8. Total phosphorus of the red blood corpuscles.

While in studies of this nature it is probably highly desirable to obtain all the samples of blood in the morning when the patients are still fasting, it proved impracticable in this work to adhere to this condition, and the collection of the samples of blood had been, therefore, made in the morning 3 to 4 hours after breakfast or in the afternoon when a similar interval of time had been allowed to elapse after the consumption of the last meal. This interval has been deemed long enough to exclude any direct influence of a meal on the partition of the phosphorus compounds of the blood.

All the specimens of blood were obtained from one of the veins of the arm except in the few infants when the longitudinal/

longitudinal sinus was the source. In order to prevent coagulation of the blood a minute quantity of potassium oxalate was used.

As very little is known at present regarding the equilibrium existing between the various forms of phosphorus in the plasma and the red blood corpuscles or the ease with which an exchange of these substances may take place between the corpuscles and plasma all the estimations were commenced immediately the sample of blood was obtained, and carried on uninterruptedly to full completion.

All the results have been obtained from triplicate estimations with only few exceptions where only duplicates have been done.

The whole technique was considered carefully, worked out, simplified, and standardised so that once the correctly measured amount of the plasma or whole blood was introduced into the pyrex boiling tubes it did not leave them till the final readings were taken in the colorimeter.

Haematocrit readings were taken from the oxalated blood which had been spun for 40-45 minutes in a centrifuge at 3000 revolutions per minute, in a centrifuge tube graduated and standardised to one tenth of a cubic centimeter.

Kay and Byrom used the substance "Heparin" as the anticoagulant in the sample of blood for the haematocrit value/



value, and potassium oxalate in that used for the estimations of the phosphorus compounds. As the substance "heparin" was not obtainable potassium oxalate was uniformly used as an anticoagulant in this work.

It is true that the osmotic pressure of potassium oxalate is relatively high, and the relative corpuscular volume probably does suffer correspondingly, but as potassium oxalate is also used for the purpose of separating plasma from the whole blood for the estimation of the phosphorus compounds the relativity is preserved, and more uniform results may be expected than those in the case of Kay and Byrom who used "heparin" for the sample of blood for the haematocrit reading, and potassium oxalate for that one used for the analysis.

(38)  
 Rossdale (1922-23) while studying haematocrit values of the blood showed that the addition to the blood of either citrate or oxalate vitiated the haematocrit readings by reducing the corpuscular volume per 100 c.c. of whole blood, unless a particular proportion of oxalate to blood be chanced upon which happens to be isotonic to the particular blood under examination. He concluded that the haematocrit value was reduced generally by 14 per cent when salts are used as compared with the values obtained from the unsalted blood samples.

The total phosphorus content of the whole blood was done in all the specimens of blood by the direct method of/

of combustion as well, and the average values agree very well with those obtained by adding together the total acid soluble phosphorus and the lipin phosphorus of whole blood. This supports Bloor's statement that forms of phosphorus other than the acid soluble phosphorus, and the alcohol-ether soluble phosphorus occur in normal blood in quite unimportant quantities. The direct and "added" totals do not always agree in the individual cases, but, it must, however, be borne in mind that the latter total is the sum of two figures each obtained independently by the process of combustion.

In most of the specimens of plasma, owing to the insufficiency of the amount available, the estimation was performed either for the lipin or total phosphorus alone, and the other figure arrived at by addition or subtraction. In the few samples where both estimations were done independently it was found that the "added" and the direct total phosphorus of plasma agreed closely.

The calcium of serum was also determined in each sample of blood, but these samples were obtained independently, and they were not oxalated.

#### The Normal Child.

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In order to find the relative normality of the partition of the phosphorus compounds in the blood, and, thus, provide a suitable standard for the quantitative estimations/

estimations in various pathological conditions, samples of blood of 10 normal children, ranging in age from 4 to 12 years, have been analysed completely.

The results of direct analysis of the whole blood, and plasma for phosphorus compounds of the 10 normal children - boys and girls - who were selected very carefully from completely convalescent patients are given in Table III. The figures for the phosphorus compounds of the red blood corpuscles have been arrived at by the process of calculation from those for the whole blood, and plasma. The highest, lowest and mean values are shown at the foot of the Table.

As the terms used here may lead to unnecessary confusion it is well to point out that all the figures are given in terms of P.

As the terms "inorganic" phosphate, and "free" phosphorus are synonymous, it is proposed to use the term "free phosphorus" throughout this paper except when quoting the figures of other workers who used other terms to designate the same thing. The term "lipin phosphorus" will be used for the alcohol-ether soluble phosphorus except when quoting the figures of other investigators who used some similar term to express the same phosphorus partition.

#### Haematocrit Findings.

The average corpuscular volume of blood in 10 normal children/

TABLE 111 - Phosphorus Compounds of the Blood in 10 Normal Children.

No.	Name.	Age.	W H O L E B L O O D.						P L A S M A					C O R P U S C L E S				Haema- tOCRIT	Serum Calcium	R.B.Cs. in millions.
			F.P.	F.E.P.	E.P.	L.P.	T.P.	T.P.	F.P.	F.E.P.	E.P.	L.P.	T. P.	F.P.	L.P.	E.P.	T. P.			
			mgm. per 100 cc.				Comb.	Add.	mgm. per 100 cc.					mgm per 100 cc.				%	mg.%	
1.	E. C.	8 yrs.	3.89	23.58	20.69	13.7	36.7	37.28	3.53	4.14	0.61	10.1	14.24	4.7	21.7	65.4	91.8	31.0	10.9	-
2.	M. McR.	12 "	4.4	29.2	24.8	13.9	43.24	43.1	4.2	4.8	0.6	8.9	13.7	4.93	25.3	80.2	110.4	30.4	-	4.8
3.	M. J.	11 "	4.1	31.4	27.3	12.9	45.1	44.3	3.9	4.37	0.47	8.53	12.9	4.47	20.9	76.9	102.27	35.1	10.08	5.1.
4.	A. McG.	11 "	4.6	30.3	26.7	14.1	43.3	44.4	4.2	4.6	0.4	10.7	15.3	5.46	20.0	71.8	97.26	36.8	11.04	-
5.	M. L.	8½ "	4.6	24.7	20.1	15.4	39.6	40.1	4.39	4.6	0.21	9.9	14.5	4.94	24.0	51.4	80.34	38.8	10.9	-
6.	M. H.	5 "	4.04	23.8	19.76	14.2	38.7	38.0	3.8	4.1	0.3	10.1	12.8	4.58	23.1	62.2	89.88	31.4	10.76	4.86
7.	J. W.	9 "	3.8	24.24	20.44	12.5	36.9	36.74	3.58	3.73	0.15	7.87	11.6	4.33	23.3	67.8	95.43	30.0	11.0	4.4
8.	T. C.	5.7/12 "	4.11	25.5	21.39	12.7	38.5	38.3	4.01	4.33	0.32	8.69	11.9	4.35	22.6	73.7	100.65	28.7	10.7	4.51.
9.	A. McF.	12 "	3.9	24.3	20.4	14.8	39.9	39.1	3.7	4.05	0.35	6.61	10.66	4.23	28.7	54.8	87.73	36.8	11.1	-
10.	A. S.	4 "	4.11	26.6	22.49	13.2	40.1	39.8	4.0	4.4	0.4	9.2	13.6	4.33	23.0	68.3	95.63	32.5	10.1	-
Average			4.15	26.36	22.4	13.74	40.2	40.11	3.93	4.31	0.38	9.06	13.12	4.63	23.26	67.25	95.13	33.15	10.73	-
Highest			4.6	30.3	27.3	15.4	45.1	44.4	4.39	4.8	0.61	10.7	15.3	5.46	28.7	80.2	110.4	38.8	11.1	-
Lowest			3.8	23.58	19.76	12.5	36.7	36.74	3.53	3.73	0.15	6.61	10.66	4.23	20.0	51.4	80.34	28.7	10.08	-



children was found to be 33.15 per 100 c.c. The highest recorded volume was 38.8, and the lowest 28.7 per 100 c.c. of blood. McKellips, De Young, and Bloor<sup>(20)</sup> (1921) reported that the whole blood of children contained on the average, 44.3 per cent of red blood corpuscles, and Kay and Byrom<sup>(3)</sup> (1927) gave an average of 43 per 100 c.c. of whole blood in the normal adults, but the latter noted the same range of fluctuation in individual cases as reported for the cases of this paper. Although, as it has been already explained elsewhere, the potassium oxalate vitiates the relative corpuscular volume of the blood it is extremely improbable that the latter would suffer to the extent of 25.1 per cent. Since the addition of minute amounts of potassium oxalate to the blood does not seem in itself sufficient to explain wholly this marked discrepancy between the corpuscular volume of blood in children and that in the adult, it is conceivable that the red blood corpuscles in children may be smaller in size than those of the adult and these two factors combined would be enough to account for the difference. In order to eliminate the possibility of secondary anaemia co-existing blood counts were done independently in 5 of the 10 normal cases, and the red blood corpuscles were found to range from 4,400,000 to 5,100,000 per cmm. It is of course self-evident that the diminution of red blood corpuscles per cmm of blood is bound to influence the corpuscular/

corpuscular volume of whole blood, but the element of size of the red blood corpuscles also exercises an appreciable influence as can be seen from Table III. The increase or decrease in the number of red blood corpuscles does not correspond to an absolutely proportionate increase or decrease in the corpuscular volume.

#### Free Phosphorus.

The average free phosphorus in 10 normal children was found to be 4.15 mg. per 100 c.c. of the whole blood, 3.93 mg. per 100 c.c. of the plasma, and 4.63 mg. per 100 c.c. of the red blood corpuscles. The highest figure recorded for the whole blood was 4.6 mg.% and the lowest 3.8 mg.%. The highest figure for the plasma was 4.39 mg. per cent, and the lowest 3.53 mg. per cent. The highest figure for red blood corpuscles was 5.46 mg. per cent, and the lowest 4.23 mg. per cent. Our average for the whole blood agrees with that arrived at by Hess and Gutman, and Riesenfeld and his co-workers, whereas some of the other investigators reported slightly higher figures, e.g. Zucker and Gutman found an average of 4.6 mg. per 100 c.c. of whole blood, and Anderson 4.8 mg. per 100 c.c. of whole blood. On the other hand, Jones and Nye reported an average of 3.1 mg. of inorganic phosphate per 100 c.c. of whole blood. The average figures for inorganic phosphate in adults are smaller than in children.

The/



The red blood corpuscles are relatively richer in free phosphorus than either the whole blood or the plasma and this agrees with the findings of Jones and Nye, and McKellip and his co-workers, and Bloor.

(19)  
Taylor and Miller (1914), on the other hand, found no inorganic phosphate in the serum. Buell (1923)<sup>(39)</sup> using Bloor's nephelometric method, found the corpuscles of the blood in the dog free of inorganic phosphates. In the corpuscles of human blood he found, however, just a trace of the inorganic phosphate, but he was of the opinion that it was due to post-mortem changes.

#### Ester Phosphorus.

The average ester phosphorus in 10 normal children was found to be 22.4 mg. per 100 c.c. for the whole blood with the highest figure of 27.3 mg., and lowest of 19.76 mg. per 100 c.c., and these findings correspond to those published by Jones and Nye; and Kay and Byrom. The actual amount of ester phosphorus in the whole blood depends entirely upon two factors: (a) the relative proportion of the red blood corpuscles to that of plasma, and (b) the amount of ester phosphorus contained actually in each red blood corpuscle at the time of the estimation.

Plasma contains very small amounts of the ester phosphorus compounds, the average amount being 0.38 mg. per 100 c.c. of plasma, the highest being 0.61 mg., and the lowest 0.15 mg. per 100 c.c. of the plasma.

It follows from the above findings that practically the whole bulk of ester phosphorus compounds is contained in the red blood corpuscles. Thus the ester phosphorus appears to be an integral constituent of the red blood cells, and it resembles haemoglobin in the reluctance with which it leaves the red blood corpuscles, little short of laking being sufficient to bring it out into the plasma.

The average ester phosphorus was found to be 67.25 mg. per 100 c.c. of the red blood corpuscles, with the highest figure of 80.2 mg. and the lowest of 51.4 mg. per 100 c.c. Strictly speaking, this is not quite correct, because the fraction of ester phosphorus of the white blood cells (leucocytes) has not been taken into account, but, in the normal individual this is so small in amount that it can be safely neglected. In the abnormal cases, however, where there is a high leucocytosis it must be allowed for.

(3 )  
Kay and Byrom (1927) termed the ester phosphorus of red blood corpuscles the "phosphorus Index", and they held that it was very constant in the normal adult. The "phosphorus index" represents the amount of ester phosphorus in milligrammes present in 100 c.c. of red blood corpuscles. According to their findings, it had practically the same value of 53 in the normal adult rarely varying in health more than 10 per cent on each side of the mean. From the results of this paper, it is 67.25 with a variation of about 20 per cent in either direction of the mean value.

As we have used the same method for estimation, it would appear that the red blood corpuscles of the blood in children are richer in ester phosphorus than those of the blood in adults.

The phosphorus index was calculated from the figures for children by Jones and Nye; and also by McKellips and his co-workers, who respectively found it to be 57.6 and 49.6. From the figures for adults published by Bloor it was calculated to be 52.9. All these investigators used the nephelometric method.

#### Lipin Phosphorus.

-oCo-

The average for the lipin phosphorus compounds of the blood is found to be 13.74 mg. per 100 c.c. of the whole blood, with the highest figure of 15.4 mg. and the lowest of 12.5 mg. per 100 c.c. The factors influencing the actual amount of lipin phosphorus compounds are much more complicated than in the case of ester phosphorus, because lipin phosphorus in contradistinction to the ester phosphorus is present in appreciable amounts both in the plasma and the red blood corpuscles though it is present in the latter  $2\frac{1}{2}$  times more than in the former.

The average lipin phosphorus of the plasma is found to be 9.06 mg. per 100 c.c., the highest being 10.7 mg. and the lowest 6.61 mg. per 100 c.c. Jones and Nye found 9.3 mg. per 100 c.c. of the plasma in children. Greenwald reported/

reported 9.82 mg. per 100 c.c. of the serum in adults, Kay and Byrom recorded an average of 7.1 mg. of the lipin phosphorus per 100 c.c. of the plasma in adults.

The average for 10 normal children of lipin phosphorus of the red blood corpuscles was found to be 23.26 mg. per 100 c.c., the highest figure being 28.7 mg., and the lowest 20.0 mg. per 100 c.c. We calculated it from the results, which were in terms of  $H_3PO_4$ , published by Jones and Nye, and McKellips and co-workers and we found it to be 19.0 mg. and 17.0 mg. per 100 c.c. of red blood corpuscles in children. Bloor reported 18.7 mg., and Kay and Byrom reported 18.0 mg. per 100 c.c. of the red blood corpuscles in adults.

It is of some importance to point out that the lipin phosphorus compounds of the red blood corpuscles, though nearly 3 times smaller in amount than the ester phosphorus, appear equally constant in the red blood corpuscles, and probably they only leave the latter under considerable stress.

Kay and Byrom while discussing the constancy of the ester phosphorus compounds of the red blood cells in health, suggested that the phosphorus compounds of blood might be grouped into two classes:-

(a) those which form a portion of the permanent furniture of the blood as tissue, and,

(b) those which are being transplanted by the blood from one organ to another.

The ester phosphorus of the red blood corpuscles of normal/

normal blood belongs mainly to the class (a). The ester phosphorus of the plasma is probably mainly of the class (b), whilst the inorganic phosphorus and the lipin phosphorus of the plasma are partly (a) and partly (b).

This tentative grouping of the phosphorus compounds of blood is incomplete in so far as the portion of lipin phosphorus of the red blood corpuscles is completely left out without any adequate explanation. As it has been sufficiently proven that the lipin phosphorus compounds fraction of the red blood corpuscles in normal blood is very constant it has the claim to be included in the permanent furniture of the blood as tissue.

#### Calcium Content of the Serum.

-oOo-

The average calcium content of the blood serum for 9 normal children was found to be 10.73 mg. per 100 c.c., the highest figure being 11.1 mg., and the lowest 10.08 mg. per 100 c.c. of the serum.

There appears to exist no evident relationship in distribution between the calcium content of serum and any compound of phosphorus in either whole blood, plasma or corpuscles from these results.

#### Summary and Conclusions.

-oOo-

1. The blood of normal children is relatively richer in phosphorus compounds than that of adults.



2. Phosphorus compounds of the blood in normal children show slightly greater variations in distribution than those of the adults.
3. The free phosphorus of blood in normal children is appreciably higher than in the adults.
4. The red blood corpuscles are richest in the free phosphorus, then the whole blood, and the plasma is poorest.
5. The plasma of the blood in normal children contains 27.6 per cent more lipin phosphorus than that of the adults.
6. The red blood corpuscles in normal children contain 29.2 per cent of lipin phosphorus more than that of the normal adults.  
The lipin phosphorus of the red blood cells is almost as constant an ingredient as is the ester phosphorus.
7. The ester phosphorus of the plasma is very small in amount.
8. The red blood corpuscles in normal children appears to be richer in ester phosphorus than those of the adults. The "phosphorus index" is not as constant in normal children as in the normal adults.
9. The calcium content of blood plasma in children was found to vary from 10.08 mg. per cent to 11.1 mg. per cent.
10. A standard for the distribution of phosphorus compounds of blood in normal children has been arrived at for reference.



P A R T III.Distribution of Phosphorus Compounds of the Blood  
in Nephritis.

-oOo-

In all the investigations of this nature the initial stumbling-block is the clinical classification of the types of nephritis to which the individual case belongs. A simple separation into (a) the acute, (b) subacute, and (c) chronic group has been adopted here. The "acute" group includes all the cases suffering from the first attack of nephritis from which apparent recovery usually follows within two months. The "subacute" group comprises all the cases with the primary attack of nephritis of more prolonged duration, in which the disease has lasted for a period of some months. The "chronic" group consists of all the cases of nephritis in which the attack is either prolonged into years or there have been recurrent attacks of the same condition.

This communication deals with 10 cases of nephritis 8 of which belong to the acute, one to the subacute, and one to the chronic group. In five patients out of the 8 suffering from acute nephritis, it was attempted to study the behaviour of phosphorus compounds of the blood during the whole course of the disease, and therefore, the samples of patients' blood were submitted to complete analysis for the phosphorus compounds at different stages of the disease. In the remaining 3 cases of acute nephritis/

nephritis as well as in the subacute one, and the chronic one complete analysis of the blood was carried out on one occasion only in each one of them.

(17)

As early as 1915 Greenwald showed that in many cases of nephritis the acid soluble phosphorus of human blood serum was markedly increased. The highest "acid soluble" phosphorus he reported was 21.1 mg. per 100 c.c. of serum. His results also showed that there was some association between phosphate retention and nitrogenous retention though not in every individual case.

(23)

Marriott and Howland (1916) studied phosphate retention as a factor in the production of acidosis in nephritis. They found that in cases of nephritis with acidosis there was an increase in the inorganic phosphate to many times the normal amount - from 8 to 23 mg. per 100 c.c. of blood. Further, they concluded that the phosphate retention, however, was not a result of acidosis per se, for they failed to find an accumulation of the inorganic phosphates in the serum of severe cases of acidosis in diabetes, and other forms of the acetone body acidosis.

(24)

Denis and Minot (1920) studied phosphate retention from the standpoint of blood analysis. Of 68 cases of cardio renal disease they analysed,  $\frac{2}{3}$  of the cases showed definite evidence of the phosphate retention. Their figures showed no definite relationship between the decrease/

decrease in the alkali reserve and the rise in the inorganic phosphate of plasma.

(41)

De Wesselow (1922-23) examined the blood of 73 nephritic patients for the inorganic phosphate, and 19 out of 73 cases showed the inorganic phosphate above 5.0 mg. per 100 c.c. of blood. Of these in 8 the inorganic phosphates exceeded 10.0 mg. per cent, in 4 it lay between 6.0 and 8.0 mg. per cent, while in the remaining 7 the inorganic phosphate level was below 6.0 mg. per cent, but above 5.0 mg. per 100 c.c. of blood. All the cases showing the inorganic phosphates over 10.0 mg. per 100 c.c. of blood died.

(42)

Denis and Hobson (1923) reported the results in 22 cases of nephritis, and cardio-renal disease, and they found the inorganic phosphates increased in 10 of them,

(50)

i.e. in 45%. Briggs (1923) also reported high inorganic phosphate values for the plasma of nephritics.

(43)

Byrom and Kay (1927) studied extensively the phosphorus compounds of human blood in renal disease. Their findings for the inorganic phosphates of blood agreed, on the whole, with those of other workers. They remarked that there was a variable, occasionally an extreme, increase in the inorganic phosphates content of whole blood or plasma. The degree of the inorganic phosphate accumulation seemed roughly proportionate to the severity of the disease as judged clinically or as assessed by the level of blood urea, and by the usual renal efficiency tests/

tests. Marked phosphorus retention appeared, however, to begin later than urea retention, and in their experience it was a very serious prognostic sign. All their cases with more than 8 mg. of the inorganic phosphates per 100 c.c. of blood died.

All the workers so far enumerated believed that the rise in inorganic phosphates of the blood was of bad prognostic import.

(44)  
Bloor (1917) studied the lipoids of the blood in nephritis, and he found abnormally high fat values in the plasma and corpuscles, and high lecithin in the corpuscles of severe nephritis. The cholesterol values were practically normal. He regarded these abnormalities as the result of a retarded assimilation of fat in the blood, which, he thought, to be one of the manifestations of a general metabolic disturbance. Epstein and Rothschild (1917), on the other hand, thought that the high lipoids in nephritis represented a condition of fat non-  
(45)  
utilization. Hiller, Linder and Lundsgaard (1924)  
(46)  
studied fat metabolism in nephritis, and they found that the nephritic patients with constant lipaemia were able to burn fat as efficiently as normal individuals. They suggested that the accumulation of fat in the blood of nephritis might be due to a disturbance in the mechanism for transferring lipoids from the blood to the tissue depots.

(17)  
Greenwald (1915) estimated the phosphorus compounds of human blood serum in nephritis, and he reported great variations in the lipoid phosphorus content. In 25 specimens of the sera in nephritics he found from 6.9 mg. to 36.2 mg. of the lipoid phosphorus per 100 c.c. of blood serum.

(47)  
Daniels (1925) reported an increase of the lipoids of plasma in 5 out of 7 cases of chronic parenchymatous nephritis examined. In the other forms of renal disorder examined no similar increase in the lipoids of plasma was found.

#### The Author's Results.

-c0o-

In all 25 complete estimations were made on the phosphorus compounds of blood in the 10 cases of nephritis studied, and the results are given in Table IV.

#### Free Phosphorus.

-c0o-

The author's results for the free phosphorus of blood in 10 nephritic children correspond, to a large extent, to those of other investigators. The highest figure recorded was 6.94 mg. per 100 c.c. of the whole blood. In all the cases there was a tendency for the free phosphorus of blood to rise above the normal average during the disease except in one case, which was suffering from acute/



Table IV.

Results of the Phosphorus Compounds of Blood in Nephritis.

Name, Age and Diagnosis	Whole Blood						Plasma					Corpuscles				Haema-	Ca.	Blood
	F.P.	F.E.P.	E.P.	L.P.	Comb. T.P.	Add. T.P.	F.P.	F.E.P.	E.P.	L.P.	T.P.	F.P.	L.P.	E.P.	T.P.	to crit. %	Serum	N.P.N.
	mgm. per 100 c.c.						mgm. per 100 c.c.					mgm. per 100 c.c.					mgm. %	mg. %
Average normal.	4.15	26.36	22.4	13.74	40.2	40.11	3.93	4.31	0.38	9.06	13.12	4.63	23.26	67.25	95.13	33.15	10.73	-
1. J. McE. aet 11 yrs	3.34	25.97	22.63	12.82	38.46	38.78	3.13	5.3	2.17	5.1	10.4	3.8	31.7	72.7	108.2	29.0	9.72	32.1
Acute Ne-	6.94	26.6	19.66	13.7	38.5	40.3	6.94	7.5	0.6	9.54	17.04	6.95	21.7	56.3	85.0	34.2	10.9	54.5
phritis, c	5.15	26.4	21.25	14.1	41.1	40.5	4.9	5.5	0.6	10.2	15.7	5.7	23.65	71.8	101.2	29.0	11.1	57.1
Uraemia	4.48	24.24	19.76	10.88	35.8	35.12	4.59	5.0	0.41	8.57	13.16	4.25	15.5	58.3	78.05	43.4	10.7	
	4.11	25.3	21.19	13.8	39.9	39.1	4.4	4.76	0.36	9.64	13.4	3.5	23.9	61.8	89.2	33.9	10.9	33.3
2. M. J. aet 6 $\frac{3}{4}$ yrs	3.11	25.64	22.53	12.25	38.2	37.89	3.68	3.47	0.39	8.65	12.12	3.2	23.29	90.4	116.89	24.6	-	84.4
Acute Ne-	4.08	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
phritis, c	4.06	26.2	22.14	13.62	38.65	39.82	3.95	4.58	0.63	11.72	16.3	4.4	19.6	90.2	114.2	24.0	-	34.0
Uraemia.	3.7	23.8	20.1	11.57	35.1	35.37	3.69	4.1	0.41	9.78	13.88	4.74	17.1	81.4	102.24	24.3	-	
3. H. J. aet 5 $\frac{1}{2}$ yrs	5.2	26.1	20.9	9.0	34.8	35.1	4.98	5.5	0.52	6.99	12.5	5.87	15.1	83.7	104.67	24.5	9.04	39.1
Acute Ne-	3.74	21.73	17.99	12.62	34.26	34.35	3.77	4.03	0.26	9.12	13.15	3.7	20.0	55.1	78.8	32.3	10.9	
phritis, c	5.1	24.2	19.1	12.07	35.84	36.27	5.38	6.15	0.77	8.06	14.08	4.4	22.3	65.7	92.4	28.2	9.76	
	4.2	22.7	18.5	11.2	33.85	33.9	4.34	4.7	0.36	7.7	12.4	3.9	18.7	57.4	80.0	31.8	9.56	
	3.83	23.5	19.67	12.9	35.9	36.4	3.89	4.2	0.31	8.5	12.7	3.69	22.8	63.6	90.1	30.6	10.2	

TABLE 1V - (continued)

Sex, Age and Diagnosis.	W H O L E B L O O D						P L A S M A					C O R P U S C L E S					Haema- tocrit	Ca Blood serum	N.P.N.
	F.P.	F.E.P.	E.P.	L.P.	Comb. T.P.	Add. T.P.	F.P.	F.E.P.	E.P.	L.P.	T.P.	F.P.	L.P.	E.P.	T.P.				
	mgm. per 100 cc.						mgm per 100 cc.					mgm per 100 cc.							
S. act 6½ yrs. Acute Nephritis	5.1	24.3	19.2	12.07	35.7	36.37	4.56	5.08	0.52	8.22	13.3	6.66	23.46	74.0	104.12	25.6	10.08	62.3	
	4.71	24.5	19.79	11.4	35.84	35.9	4.59	4.8	0.21	7.68	12.66	4.96	19.3	61.7	85.96	31.8	9.6	-	
	4.1	24.2	20.1	13.1	37.56	37.3	3.92	4.35	0.43	8.9	13.15	4.58	24.07	71.4	100.05	27.7	-	44.4	
McC act 9½ yrs. Acute Nephritis	5.8	26.1	20.3	13.28	39.87	39.38	5.73	6.05	0.32	8.41	14.46	5.9	22.2	57.0	85.1	35.2	9.84	43.5	
	4.96	27.2	22.24	14.1	41.6	41.3	4.8	5.42	0.62	9.28	14.7	5.28	23.59	64.39	93.26	33.9	9.3	31.6	
	4.1	26.8	22.7	13.5	40.49	40.3	3.93	4.4	0.43	9.27	13.67	4.5	22.0	67.9	94.4	33.0	10.7	30.1	
D. act 8 yrs. Acute Nephritis.	4.96	26.3	21.34	13.18	40.79	40.1	4.73	4.99	0.26	9.16	14.15	5.33	20.0	57.0	82.33	37.1	9.26	-	
H. act 3½ yrs. Acute Nephritis.	5.2	28.6	21.4	13.9	40.87	40.5	5.0	5.4	0.4	10.1	15.5	5.8	23.0	72.0	100.8	29.3	8.8	71.8	
M. act 12½ yrs. Acute Nephritis.	4.13	24.7	20.54	8.95	33.6	33.65	3.55	3.78	0.23	6.02	9.8	5.1	14.2	56.9	76.2	35.8	8.07	-	
W. act 12 years Chronic Nephritis	4.5	27.21	22.71	10.3	37.23	37.51	4.28	4.64	0.36	10.05	14.69	4.9	10.7	63.8	79.4	35.2	9.86	-	
McB act 11½ yrs. Subacute Nephritis	4.5	26.6	22.1	13.9	40.16	40.5	4.4	5.03	0.63	12.27	17.3	4.7	17.8	74.4	96.9	29.1	9.6	-	

F.P. - Free phosphorus; F.E.P. - Free & Este Phosphorus; L.P. Lipin phos. T.P. - total phosphorus.

F.P. - Free phosphorus; F.E.P. - Free &amp; Este Phosphorus; L.P. Lipin phos. T.P. - total phosphorus.

acute nephritis with symptoms of uraemia, in which the free phosphorus of blood failed to rise above that of the normal average throughout the disease. Analysis of the blood for free phosphorus was done on three different occasions during the course of disease, and once during the convalescent stage, and the free phosphorus of blood was never found above the normal average.

In most of the instances where both the free phosphorus and the non-protein nitrogen of blood were estimated at the same time it was found that the increase in free phosphorus and non-protein nitrogen retention co-existed though not invariably. There were instances where either the free phosphorus of blood or non-protein-nitrogen retention of blood was present alone. Thus case 2 suffering from an attack of acute nephritis with definite symptoms of uraemia showed non-protein nitrogen retention of 84.4 mg. per 100 c.c. of blood whereas there was no increase in the free phosphorus of blood recorded throughout the disease. Similarly Case 3, which was also suffering from acute nephritis, the state of affairs was noted to be the reverse of that in case 2: the free phosphorus of blood was above 5 mg. per cent, and the non-protein nitrogen retention of blood was only 39.1 mg. per 100 c.c. of blood.

The cause of these differences in the degree of an increase in the free phosphorus, and the non-protein nitrogen retention of blood in nephritis has not been explained satisfactorily/

satisfactorily, and, in all probability, there is more than one factor responsible.

(1) They may be the result not so much of variations in excretion as of variations in the diet, and in the demand for phosphorus and nitrogen for anabolic purposes.

(2) There may be different mechanisms in the kidney for the excretion of waste products, namely phosphates and urea, and these mechanisms may be, but need not be, impaired or damaged at the same time.

(3) Non-protein nitrogen retention in the blood may be due to the damage of the kidney, and the rise of the free phosphorus of blood may be due to the impairment of the regulating mechanism for the synthesis of ester phosphorus compounds in the blood.

(41)  
De Wesselow (1923) pointed out that inorganic phosphate retention was apparently more definitely connected with the symptoms of uraemia than was the non-protein nitrogen retention, but neither of our 2 cases of acute nephritis with symptoms of uraemia would lend much support to his statement. Thus case 1 was admitted with marked symptoms of uraemia following acute nephritis. Both the free phosphorus and non-protein nitrogen of blood were estimated at once, and it was found that there was neither an increase in the free phosphorus nor non-protein nitrogen per 100 c.c. of blood. The actual figures were 3.34 mg. of the free phosphorus, and 32.1 mg. of non-protein nitrogen/



nitrogen per 100 c.c. of blood. But, however, on the third day after admission, while the symptoms of uraemia were still as evident, the analysis of blood was repeated, and there was found a marked rise both in the free phosphorus and non-protein nitrogen of the blood. The free phosphorus rose to 6.94 mg. and the non-protein nitrogen to 54.5 mg. per 100 c.c. of blood. This case apparently showed that the manifestation of symptoms of uraemia could precede both the increase of the free phosphorus and of the non-protein nitrogen of the blood.

On the other hand, case 2 which was also suffering from acute nephritis with definite symptoms of uraemia showed no increase in the free phosphorus of the blood whereas the non-protein-nitrogen was markedly increased. In fact, the free phosphorus of blood was 3.11 mg. per 100 c.c. of blood which is even below that of the normal average. The non-protein-nitrogen was 88.4 mg. per 100 c.c. of blood.

De Wesselow also suggested that the phosphatic retention involved certain deleterious results which our findings in the cases 1 and 2 did not seem to support.

(48)  
Greenwald (1918) studied the supposed toxicity of sodium phosphate, and he concluded that there was no evidence of direct toxic action of the phosphate ions.

In the series of 5 cases suffering from acute nephritis in which the analysis of blood for the phosphorus compounds was/



was performed on more than one occasion during the disease it is of interest to note that in 4 cases out of 5 the free phosphorus of the blood was highest during the most acute stage of the disease, and as the condition improved this increase in the free phosphorus of blood showed tendency to taper off (Chart I). In the other case (No.2) there was no increase in the free phosphorus of the blood above the normal average, but still there was a slight variation in the amount at different stages of the examination.

The free phosphorus curve could be fairly well correlated with the clinical condition, but the free phosphorus of blood took a longer time to come down to the normal level than the clinical signs and symptoms, for at the time of dismissal when the patients were cured clinically the free phosphorus of the blood was still slightly above the normal. At some interval after dismissal, when the estimations were repeated, the free phosphorus level was found to be within the limits of normality.

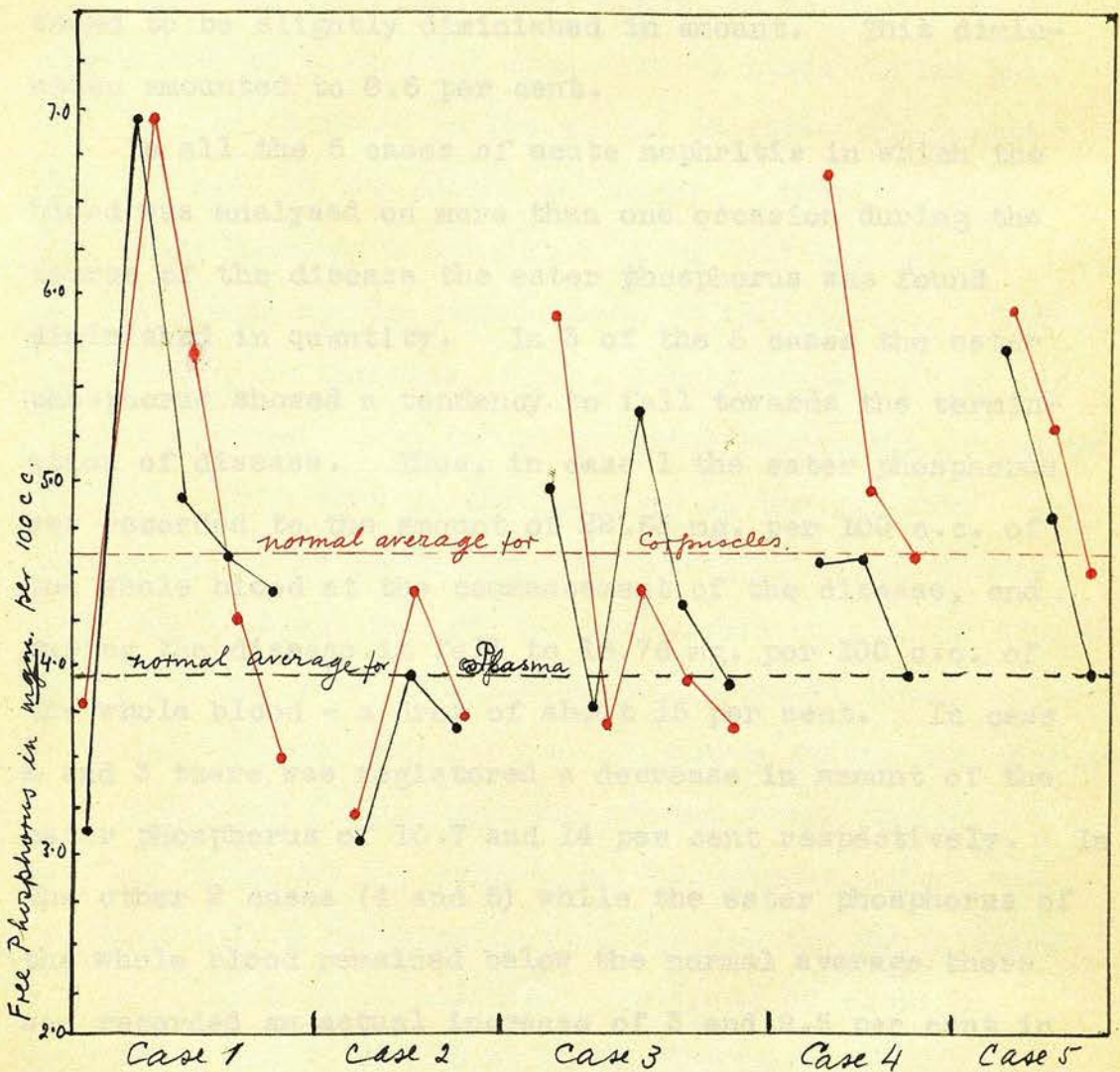
Another minor observation noted was that there was not only a relative disturbance of the free phosphorus of whole blood, plasma, and corpuscles in nephritis, but also a general one. In the normal children the free phosphorus in milligrammes per 100 c.c. of whole blood, plasma, and corpuscles was invariably highest in the corpuscles, next in the whole blood, and lowest in the plasma, whereas in the/

# Chart I

Variation in Free Phosphorus of Blood in different cases of Acute Nephritis.

— Free Phosphorus of Plasma

— Free Phosphorus of Corpuscles



the nephritic children this order was often found disturbed.

### Ester Phosphorus.

-c0o-

Whole Blood: The average ester phosphorus of 19 different samples of the whole blood in nephritis was found to be slightly diminished in amount. This diminution amounted to 8.6 per cent.

In all the 5 cases of acute nephritis in which the blood was analysed on more than one occasion during the course of the disease the ester phosphorus was found diminished in quantity. In 3 of the 5 cases the ester phosphorus showed a tendency to fall towards the termination of disease. Thus, in case 1 the ester phosphorus was recorded to the amount of 22.63 mg. per 100 c.c. of the whole blood at the commencement of the disease, and during the disease it fell to 19.76 mg. per 100 c.c. of the whole blood - a drop of about 15 per cent. In case 2 and 3 there was registered a decrease in amount of the ester phosphorus of 10.7 and 14 per cent respectively. In the other 2 cases (4 and 5) while the ester phosphorus of the whole blood remained below the normal average there was recorded an actual increase of 3 and 9.5 per cent in the amount during the course of the disease.

Plasma: The average ester phosphorus of 19 different specimens of the plasma in nephritis was found to be increased/



increased in amount by 39.5 per cent. The actual average amount of the ester phosphorus was found to be 0.53 per 100 c.c. of the plasma. Our finding agrees with that of Byrom and Kay who gave an average value of 0.5 mg. of ester phosphorus per 100 c.c. of the plasma in nephritis.

In 4 out of 5 individual cases, in which the ester phosphorus of plasma was done several times during the disease, an increase in the amount of ester phosphorus per 100 c.c. of the plasma was found. Thus, in case 1 the ester phosphorus was found to be 2.17 mg. per 100 c.c. of the plasma at the commencement of the disease. This is actually an increase of more than 5 times that of the normal average. The amount of ester phosphorus of plasma gradually fell towards the recovery of the patient. In case 2 the ester phosphorus fluctuated in amount between 0.39 and 0.63 mg. per 100 c.c. of plasma during the disease. In case 3 the ester phosphorus oscillated in amount between 0.26 and 0.77 mg. per 100 c.c. of plasma during the disease.

Red Blood Corpuscles: The average ester phosphorus or what Byrom and Kay termed the "phosphorus index" was calculated from the results obtained for the whole blood and the plasma of 19 different specimens of blood in nephritis, and it was found to be 67.51 mg. per 100 c.c. of the red blood corpuscles. This was only about 0.4 per cent higher than that given for the normal average in children/

children, but the oscillation in the amount was found to be greater in the case of nephritis than in the normal. This figure of the average ester phosphorus of the red blood corpuscles in nephritis would negative any suggestion that there was an accumulation in the amount of the ester phosphorus in the red blood corpuscles during the disease, but in 4 out of 5 cases, in which the blood analysis was done on several occasions during the disease, the ester phosphorus of the red blood corpuscles was found to be greater in amount at the onset of the disease than the normal average. In these 4 cases the earliest estimations of the blood for phosphorus compounds yielded figures of 72.7, 90.4, 83.7, and 74.0 mg. of the ester phosphorus per 100 c.c. of red blood corpuscles respectively. During the course of nephritis the ester phosphorus or the so-called "phosphorus index" of the red blood corpuscles fluctuated in the same patient, and with complete recovery approached the level of normality. For instance, in case 1, in which 5 different estimations of the blood were carried out during the disease, the ester phosphorus varied in amount from 56.3 to 72.7 mg. per 100 c.c. of red blood corpuscles being 61.8 mg. per cent a few months after complete recovery. Case 3 showed a variation between 55.1 and 83.7 mg. of ester phosphorus per 100 c.c. of the red blood corpuscles, and one month after recovery the ester phosphorus was 63.6 mg. per cent, which is within the limits of normality. This inconsistency of/



of the ester phosphorus or the so-called "phosphorus index" supported the findings of Byrom and Kay.

Our findings in the individual cases forcibly suggested that the "regulating mechanism" of the ester phosphorus in the red blood corpuscles in nephritis was altered, for at certain stages of the disease the red blood corpuscles seemed to be called upon to accommodate a greater amount of the ester phosphorus per unit cell, and at others they released the ester phosphorus at a quicker rate.

#### Lipin Phosphorus.

-oOo-

Whole Blood: The average lipin phosphorus of 19 different specimens of whole blood in nephritis was found to be 12.22 mg. per cent. It was 11 per cent below that of the normal average.

In 5 cases in which the lipin phosphorus was determined on several occasions during the disease, it was found to be diminished in the amount at the commencement of the disease. During the disease it showed a tendency to rise appreciably in amount; in the last stage of the disease it fell again; and at the end of complete recovery regained the limits of normality. Thus in case 1 the lipin phosphorus was found to be 12.82 mg. per 100 c.c. of the whole blood at the onset, and then during the disease it rose gradually to 14.1 mg. per c.c. of whole blood/

blood. Afterwards it fell to 10.88 mg. and on complete recovery it rose again to 13.8 per 100 c.c. of the whole blood. The lipin phosphorus of whole blood of all the other cases showed a similar tendency which can be seen in Chart II. and II.A.

Plasma: The average lipin phosphorus obtained from the results of 19 different estimations of the blood plasma in nephritis was 8.77 mg. per 100 c.c. of the plasma, i.e. it was 3 per cent below the normal average.

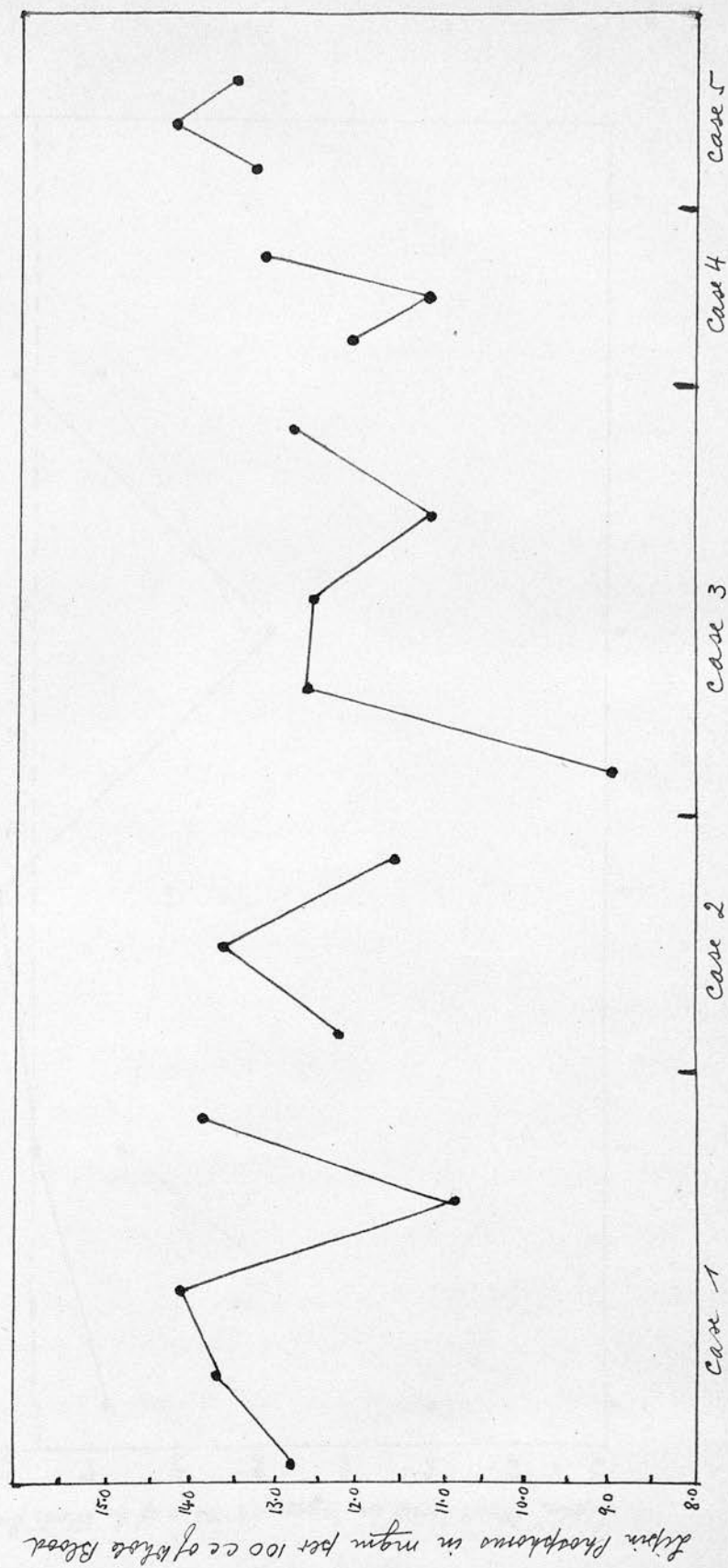
In the individual cases the lipin phosphorus of plasma showed a tendency to fluctuate, and in 2 out of 5 cases it was found to be very low in amount per 100 c.c. of the plasma at the commencement of the disease. Thus in Case 1 a variation from 5.1 to 10.2 mg. of the lipin phosphorus per 100 c.c. of plasma was revealed during the course of the disease. In case 2 it varied from 8.65 to 11.72 mg. per 100 c.c. of plasma, and in case 3 from 6.99 to 9.12 mg. per 100 c.c. of the plasma. Chart III.

Red Blood Corpuscles: The average of lipin phosphorus as calculated from 19 complete estimations of blood in nephritis was found to be 20.3 mg. per 100 c.c. of the red blood corpuscles. This amount was 12.7 per cent below the normal average. The fluctuation of the lipin phosphorus of the red blood corpuscles in nephritic children was much greater than that of the normal children.

In the individual cases the fluctuation of the lipin phosphorus in amount per 100 c.c. of red blood corpuscles was/

## Chart II

Showing a curve in the Lipin Phosphorus of Blood in different cases of  
Acute Nephritis

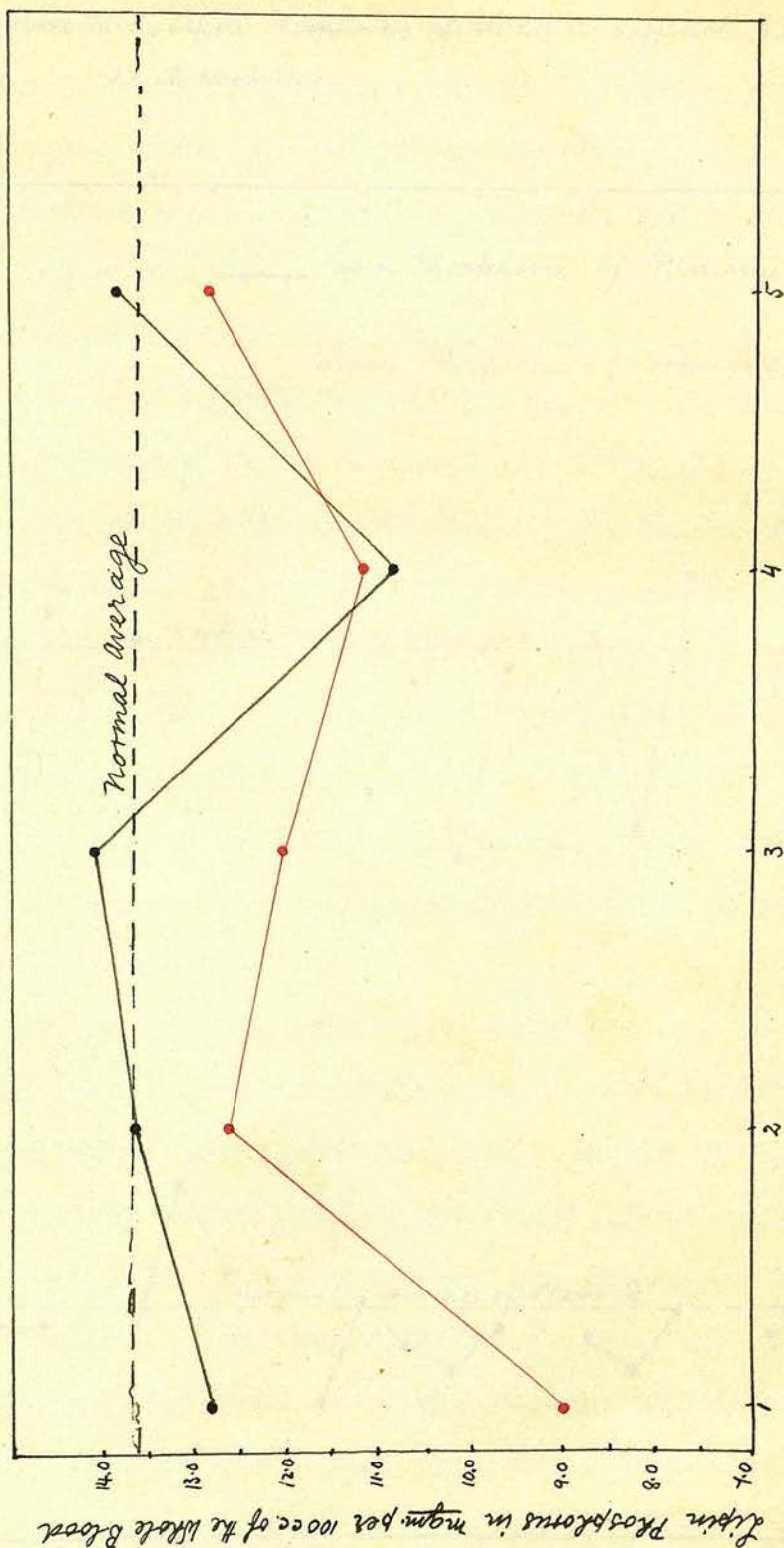


# Chart II.A.

Showing fluctuation in the Lipin Phosphorus content of the Blood during the Course of Acute Nephritis.

— Case 1

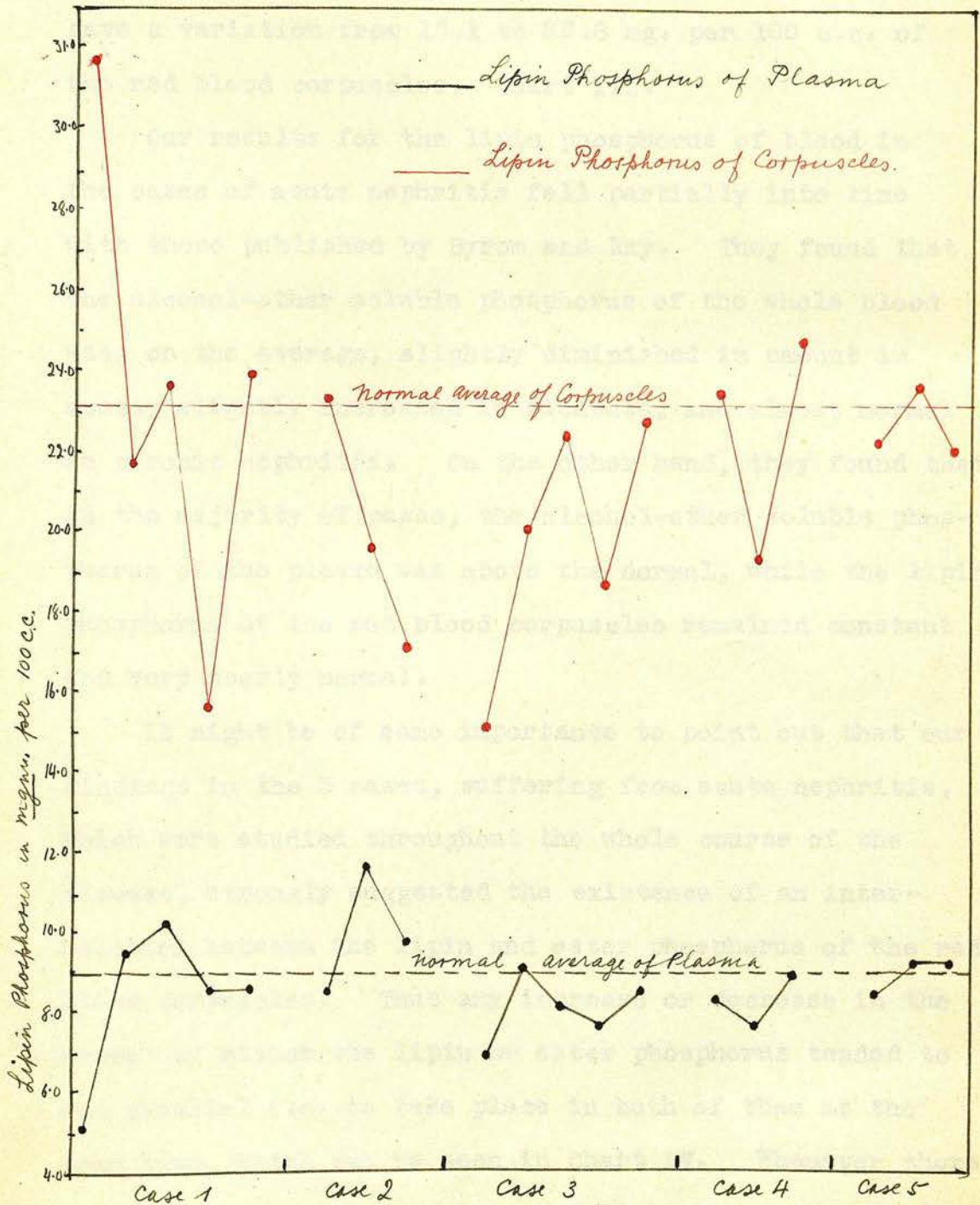
— Case 2





### Chart III

Showing a curve in the Lipin Phosphorus of Blood in different cases of Acute Nephritis





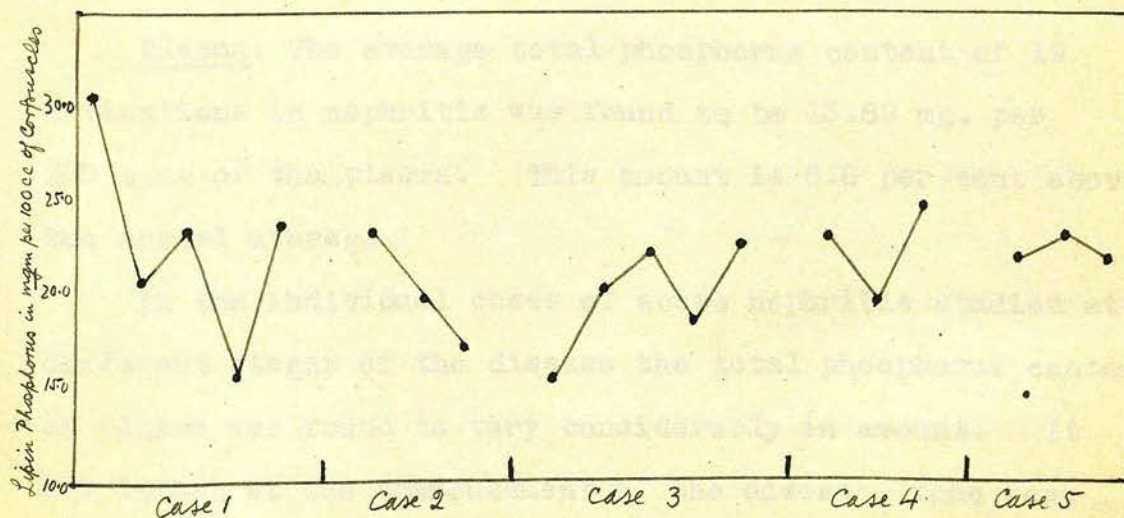
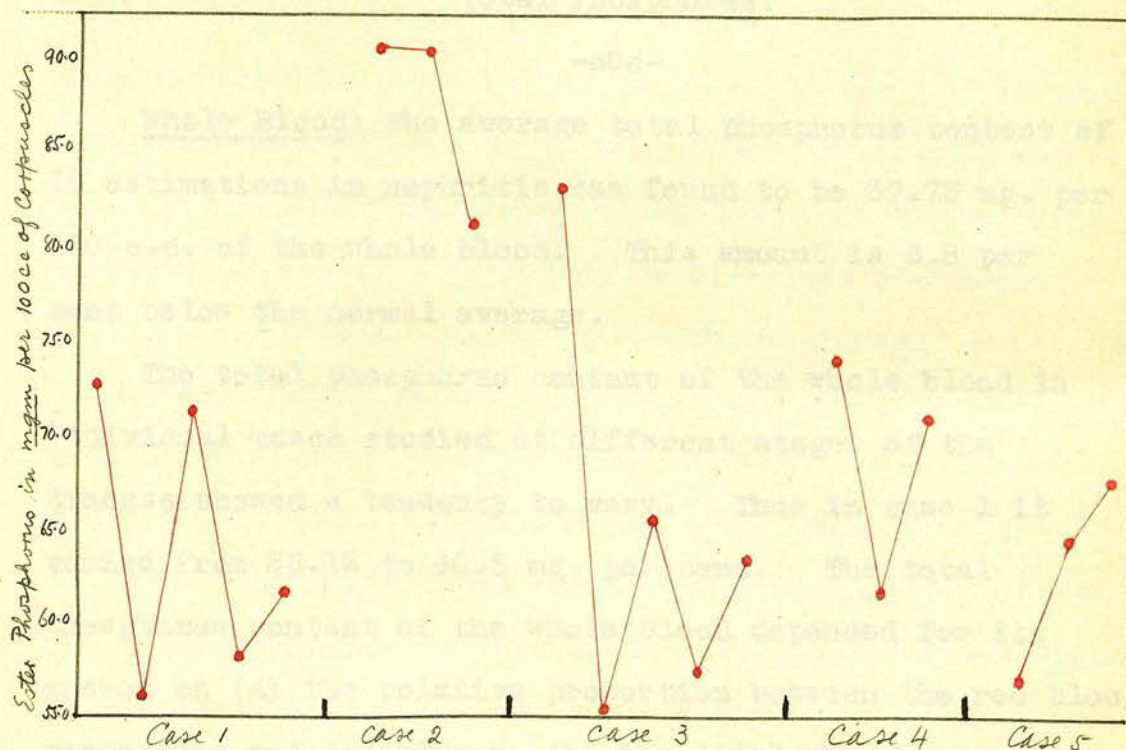
was very marked. Thus case 1 showed a variation in amount from 15.0 to 31.7 mg. of the lipin phosphorus per 100 c.c. at different stages of the disease. Case 3 gave a variation from 15.1 to 22.8 mg. per 100 c.c. of the red blood corpuscles. Chart III.

Our results for the lipin phosphorus of blood in the cases of acute nephritis fell partially into line with those published by Byrom and Kay. They found that the alcohol-ether soluble phosphorus of the whole blood was, on the average, slightly diminished in amount in acute, slightly increased in subacute, and almost normal in chronic nephritis. On the other hand, they found that, in the majority of cases, the alcohol-ether soluble phosphorus of the plasma was above the normal, while the lipin phosphorus of the red blood corpuscles remained constant and very nearly normal.

It might be of some importance to point out that our findings in the 5 cases, suffering from acute nephritis, which were studied throughout the whole course of the disease, strongly suggested the existence of an inter-relation between the lipin and ester phosphorus of the red blood corpuscles. Thus any increase or decrease in the amount of either the lipin or ester phosphorus tended to run parallel i.e. to take place in both of them at the same time, which can be seen in Chart IV. Whenever there happened to be either a rise or fall in the ester phosphorus of red blood corpuscles a similar change was registered in/

# Chart IV

Showing Simultaneous Fall and Rise in Lipin and Ester Phosphorus of Red Blood Corpuscles in different cases of Acute Nephritis



in the lipin phosphorus of the red blood corpuscles as well.

### Total Phosphorus.

-oOo-

Whole Blood: The average total phosphorus content of 19 estimations in nephritis was found to be 37.75 mg. per 100 c.c. of the whole blood. This amount is 5.8 per cent below the normal average.

The total phosphorus content of the whole blood in individual cases studied at different stages of the disease showed a tendency to vary. Thus in case 1 it varied from 35.12 to 40.5 mg. per cent. The total phosphorus content of the whole blood depended for its amount on (a) the relative proportion between the red blood corpuscles and the plasma, (b) the total phosphorus content of the plasma portion, and (c) the total content of the red blood corpuscles portion.

Plasma: The average total phosphorus content of 19 estimations in nephritis was found to be 13.89 mg. per 100 c.c. of the plasma. This amount is 5.8 per cent above the normal average.

In the individual cases of acute nephritis studied at different stages of the disease the total phosphorus content of plasma was found to vary considerably in amount. It was lowest at the commencement of the disease, then rose appreciably during the disease and returned to the limits of/

of normality when recovery was complete. These changes were especially marked in cases 1 and 2.

Red Blood Corpuscles: The average total phosphorus content of 19 estimations of blood in nephritis was calculated to be 92.8 mg. per 100 c.c. of the red blood corpuscles, which is 2.4 per cent below the normal average.

In the individual cases of acute nephritis in which several observations were made on different occasions during the disease, the total phosphorus content was found very much increased in amount per 100 c.c. of the red blood cells. Thus in cases 1, 2, 3, and 4 it was found to be 108.2, 116.89, 104.67, and 104.12 mg. per 100 c.c. of the red blood corpuscles respectively. During the disease it decreased in amount with marked fluctuation. As the recovery set in the total phosphorus content of the red blood corpuscles returned to the limits of normality.

#### Haematocrit Finding.

-oOo-

The average percentage of the red blood corpuscles of 19 observations in nephritis was found to be 30.7 c.c. per 100 c.c. of whole blood. It was 7.3 per cent below the normal average.

In 4 of the 5 cases in which several observations were made during the disease an appreciable fluctuation was noted.



Calcium of the Blood Serum in Nephritis.

-000-

(23)

Marriott and Howland (1916) reported a marked reduction of calcium in the blood serum in nephritis. They found in one case only 1.5 mg. of the calcium per 100 c.c. of serum. They assigned this low calcium to the excess of the inorganic phosphates in the serum. Halversan, Mohler, and Berghein <sup>(49)</sup> (1917) also found low calcium values in the specimens of nephritic serum. Their lowest value was 6.8 mg. of calcium per 100 c.c. of the serum. De Wesselow <sup>(41)</sup> (1922-23) found that in the acute nephritis the reduction of the calcium content below 9 mg. per 100 c.c. of serum was not uncommon. In 11 out of 142 observations the calcium content was below 7.0 mg. per 100 c.c. of the serum, and the lowest figure recorded was 5.1 mg. per 100 c.c. Denis and Hobson reported a reduction in the calcium content of serum in 5 out of 22 cases examined. Briggs <sup>(50)</sup> (1923) also reported low calcium values for nephritis. Schmitz, Rohdenburg, and Myers <sup>(51)</sup> (1926) studied the inorganic phosphate and the calcium content of blood serum in nephritis, and they found that a relatively high percentage of cases of chronic interstitial nephritis with muscular twitchings or convulsions showed values for calcium of the blood serum below 7.0 mg. per cent.

We made 20 observations on the calcium content of the blood serum in the cases of nephritis studied and we found/

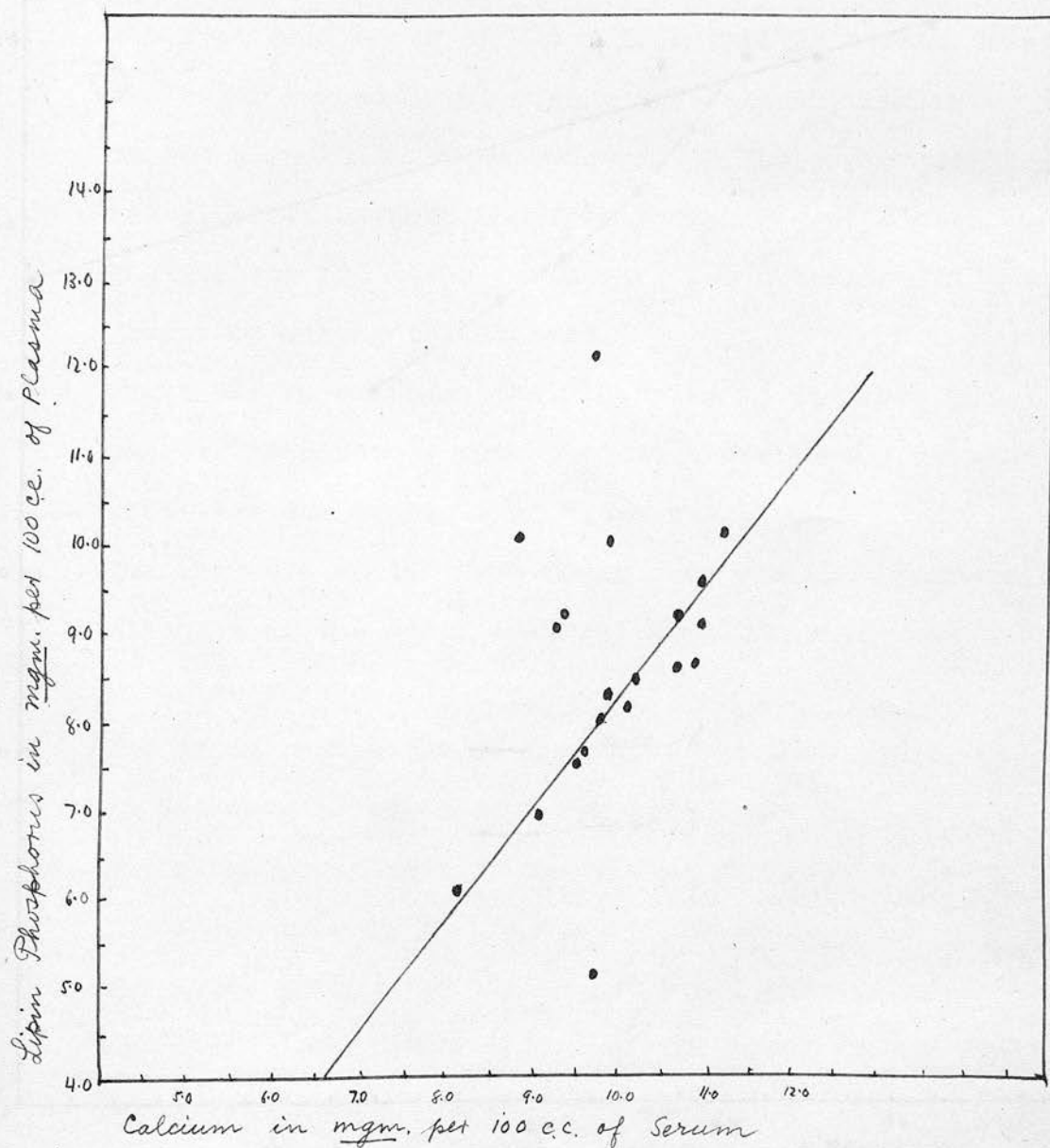
found a slight tendency for the calcium content to decrease in amount per 100 c.c. of the blood serum, the lowest value recorded being 8.07 per 100 c.c. of serum.

In the individual case studied in which the calcium content of the blood serum was estimated on several occasions during the disease we failed to find any relationship between the free phosphorus and calcium content. Binger (1917-18)<sup>(52)</sup> found that injections of the phosphoric acids and its salts in the dog produced a fall in the calcium content to a level of 6.0 mg. per 100 c.c.<sup>(53)</sup> of the serum. Tisdall (1922) observed a similar diminution of the calcium content in serum as the result of the injection of sodium phosphate and phosphoric acid. But neither of them assigned this reduction in the calcium to the accumulation of the inorganic phosphates in the serum.

On the other hand, our results showed some evidence in support of a relationship existing between the lipin phosphorus content of the plasma and the calcium content of the serum, which can be seen in Chart V. This interrelation was evident in the different cases and more so in the individual ones in which both the lipin phosphorus content, and the calcium content were done simultaneously on more than one occasion during the disease. The lipin phosphorus content of plasma, and the calcium content of serum either increase or decrease together and proportionately, i.e. the smaller the amount of the lipin phosphorus/

### Chart V.

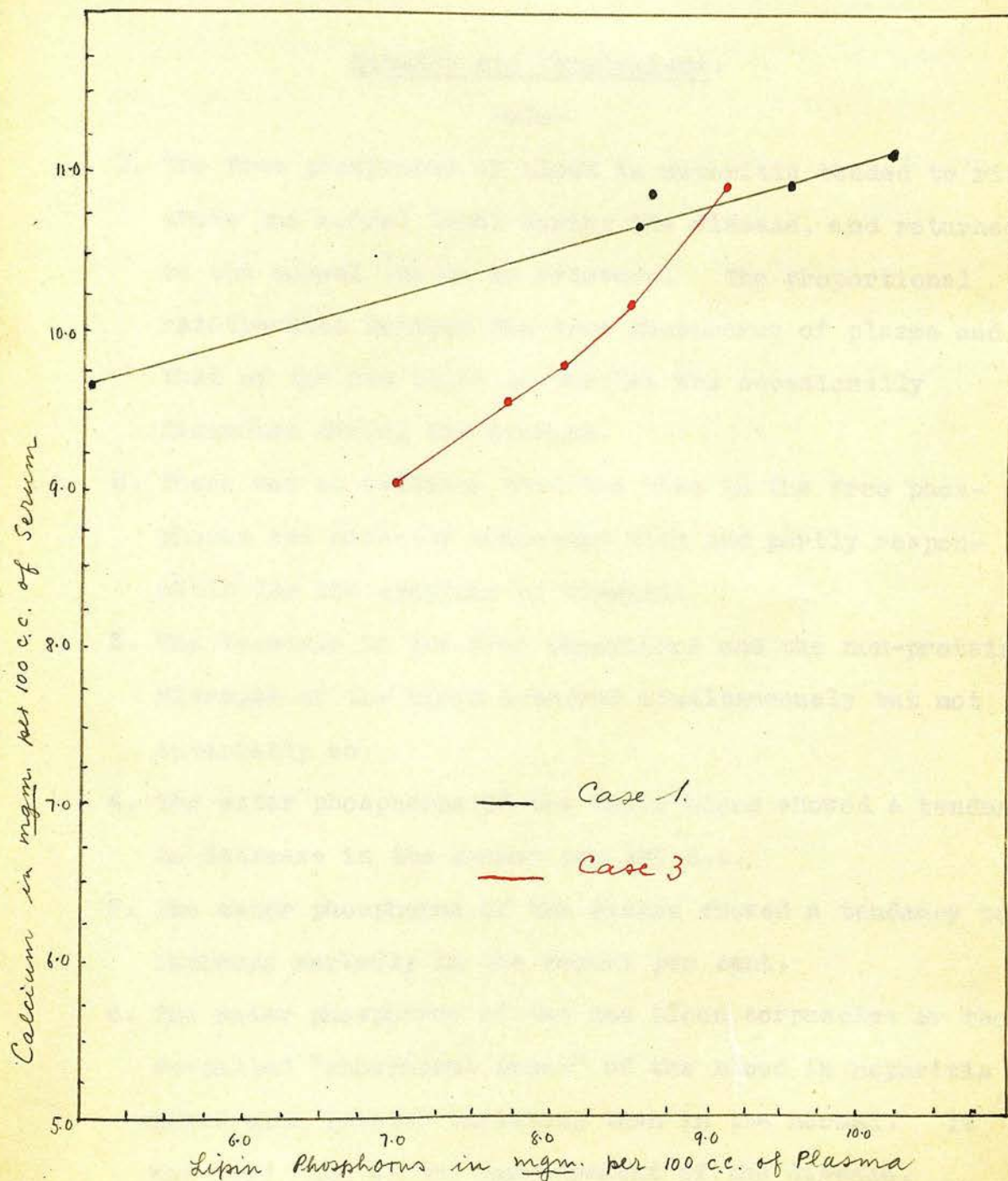
Showing the Relationship between the Lipin Phosphorus of Plasma and Calcium content of Serum in Nephritis



Not  
convincing

# Chart VI

Showing Relationship between the Lipin Phosphorus of Plasma and Calcium content of Serum in two cases of Acute Nephritis





phosphorus the smaller was the amount of calcium per 100 c.c. of the plasma or serum and vice versa. The ratio however appeared to be different for each individual case. See Charts. Chart VI.

### Summary and Conclusions.

-oOo-

1. The free phosphorus of blood in nephritis tended to rise above the normal level during the disease, and returned to the normal limits on recovery. The proportional relationship between the free phosphorus of plasma and that of the red blood corpuscles was occasionally disturbed during the disease.
2. There was no evidence that the rise in the free phosphorus was directly connected with and partly responsible for the symptoms of uraemia.
3. The increase in the free phosphorus and the non-protein nitrogen of the blood occurred simultaneously but not invariably so.
4. The ester phosphorus of the whole blood showed a tendency to decrease in the amount per 100 c.c.
5. The ester phosphorus of the plasma showed a tendency to increase markedly in the amount per cent.
6. The ester phosphorus of the red blood corpuscles or the so-called "phosphorus index" of the blood in nephritis showed much greater variation than in the normal. It was very high at the commencement of the disease.

7. The lipin phosphorus of the whole blood, and the plasma showed an appreciable variation in amount during the disease.
  8. The lipin phosphorus of the red blood corpuscles underwent a marked fluctuation during the disease.
  9. There was evidence of a relationship between the lipin phosphorus and the ester phosphorus of the red blood corpuscles. Both of them showed a tendency either to increase or decrease in the amount at the same time.
  10. There was a slight tendency for the <sup>calcium</sup> clacium content of the blood serum to be diminished.
  11. There was evidence of definite relationship between the lipin phosphorus of the plasma and the calcium content of the serum in nephritis.
-

Distribution of Phosphorus Compounds of the Blood  
in Diabetes Mellitus.

-oOo-

Diabetes Mellitus being a metabolic disease - primarily of the carbohydrate metabolism - it was considered opportune to undertake the study of the partition of the phosphorus compounds of the blood in children suffering from that pathological condition.

Evidence has been forthcoming gradually to suggest that the organic and inorganic compounds of the phosphorus of the blood were intimately concerned in the normal metabolism of the carbohydrates. For instance, it is well known that the concentration of the inorganic phosphate shows a tendency to fall noticeably after a meal, and to remain below the fasting level for a few hours. Further, (54) Wigglesworth, Woodrow, Smith, and Winter (1923) showed that the injection of insulin into a rabbit caused a rapid fall in the inorganic phosphate per 100 c.c. of the blood. (55) Bollinger and Hartman (1925) found that this fall in the inorganic phosphate was accompanied by a parallel diminution in the excretion of the inorganic phosphate in the urine.

(56) Harrop and Benedict (1924) studied the distribution of the inorganic phosphate in the body after the administration of insulin and glucose, and they found a decrease in amount of the inorganic phosphate per 100 c.c. of blood, and an increase in the muscle. At the same time they/

they found a diminished excretion of the inorganic phosphate in the urine.

(57)  
Friedlander and Rosenthal (1926) published some interesting results in connection with diabetes mellitus. They injected alkaline sodium phosphate intravenously both in the diabetic and normal subjects, and they noticed a fall in the glucose concentration of the blood lasting for several hours in the diabetics, whereas in the normal control subjects no change was recorded. They were led to infer from these observations that, as the respiratory quotient remained unaltered, synthesis of the inorganic phosphate and glucose to the hexose-phosphate had occurred somewhere in the body.

#### Author's Results.

-oOo-

Owing to this condition being comparatively rare in early life only 4 children suffering from diabetes mellitus were available for this purpose, and in 3 of them it was attempted to make several independent estimations of the phosphorus compounds of blood during their sojourn in the hospital. The distribution of the phosphorus compounds of blood is given in Table V.

#### Free Phosphorus.

-oOo-

Whole Blood: The average free phosphorus of 11 estimations in 4 cases of diabetes mellitus was found to be 3.54/



TABLE V - Results of the Phosphorus Compounds in  
Diabete Mellitus.

NAME, AGE & DIAGNOSIS	W H O L E B L O O D						P L A S M A					C O R P U S C L E S.				Haema- tocrit	Ca. Serum
	F.P.	F.E.P.	E.P.	L.P.	Comb. T.P.	Add. T.P.	E.P.	F.E.P.	E.P.	L.P.	T.P.	F.P.	L.P.	E.P.	T.P.		
			mgn. per 100 cc.					mgn. per 100 cc.				mgn. per 100 cc.				R.B.Cs%	mg.%
Normal Average.	4.15	26.36	22.4	13.74	40.2	40.11	3.93	4.31	0.38	9.06	13.12	4.63	23.26	67.25	95.13	33.15	10.73
L. aet 5 $\frac{1}{2}$ yrs. abetes Mellitus	3.0	24.4	21.4	9.1	34.0	33.5	2.85	3.56	0.71	7.7	11.26	3.3	11.7	60.1	75.1	34.8	9.9
	3.3	27.4	24.1	8.9	37.6	36.3	3.25	4.02	0.77	8.88	12.9	3.4	8.9	63.8	76.1	37.0	11.2
	3.5	22.2	18.7	14.9	37.4	37.1	4.2	4.29	0.09	9.61	13.9	1.96	26.89	60.9	89.75	30.6	9.1
J.B. aet. 10 $\frac{3}{4}$ yr abetes Mellitus	3.8	24.0	20.2	10.4	34.2	34.4	3.9	4.1	0.2	12.0	16.1	3.63	7.35	58.3	69.28	34.4	10.3
	3.17	25.3	22.13	14.8	39.75	40.1	3.22	3.68	0.46	14.52	18.2	3.0	15.3	63.5	81.8	34.5	10.1
	3.4	21.53	18.13	12.98	34.72	34.51	3.28	3.6	0.32	10.88	14.48	3.63	17.24	54.3	75.17	33.0	10.8
J. McK aet 8 $\frac{1}{2}$ years abetes Mellitus	3.48	28.7	25.22	12.9	41.4	41.6	3.15	3.65	0.5	11.25	14.9	4.15	16.2	75.4	95.75	33.0	12.3
	3.49	25.83	22.34	11.26	37.45	37.09	3.51	3.8	0.29	8.85	12.65	3.4	16.4	69.4	89.2	31.9	10.8
	4.11	24.06	19.95	10.22	34.52	34.28	4.22	4.54	0.32	8.96	13.5	3.9	12.5	55.4	71.8	35.6	11.2
	4.2	26.7	22.5	12.36	39.3	39.06	4.4	4.75	0.35	8.35	13.1	3.85	19.3	61.37	84.52	36.3	11.0.
J. A.G. aet 10 years abetes Mellitus.	3.54	23.46	19.92	8.4	32.05	31.86	3.48	3.98	0.5	5.86	9.85	3.65	12.5	51.8	67.95	37.8	10.47

F.P. - Free Phosphorus; F.E.P. - Free plus Este Phosphorus; L.P. - Lipin Phosphorus; T.P. Total Phosphorus.

3.54 mg. per 100 c.c. of the whole blood. This amount was about 15 per cent below the normal average. Only in 2 out of 11 observations the free phosphorus of the whole blood reached the normal level, but, however, both of these observations were made on the same patients, and that during the latter part of the disease, i.e. when the condition was comparatively well under the dietary and insulin control.

In 2 out of 3 cases in which estimation of the phosphorus compounds of blood were carried out on more than one occasion in each individual case during their treatment in the hospital, there was noticed a tendency for the inorganic phosphorus to increase in amount per 100 c.c. of the whole blood as the metabolic disturbance of the carbohydrates was righted by means of careful dieting and insulin therapy. This rise was gradual, in one case just reaching the normal level, and in the other falling short of it.

This diminution of the free phosphorus was difficult to explain, but it might be due to polyuria accompanying the condition of diabetes mellitus, during which a relatively greater amount of the free phosphorus was excreted as waste product.

Our findings of a distinct fall in the free phosphorus of the whole blood in diabetes mellitus did not agree with those of Byrom (1929)<sup>(58)</sup>, who reported that there was no change in the concentration of the free phosphorus of the blood/

blood in diabetic adults until coma supervened when the level of concentration rose considerably.

Plasma: In 9 out of 11 estimations the free phosphorus of the plasma was found appreciably lower in amount per 100 c.c. than that of the normal average in children. In the other 2 cases, however, it was found to be just slightly above the normal average. See Chart VII.

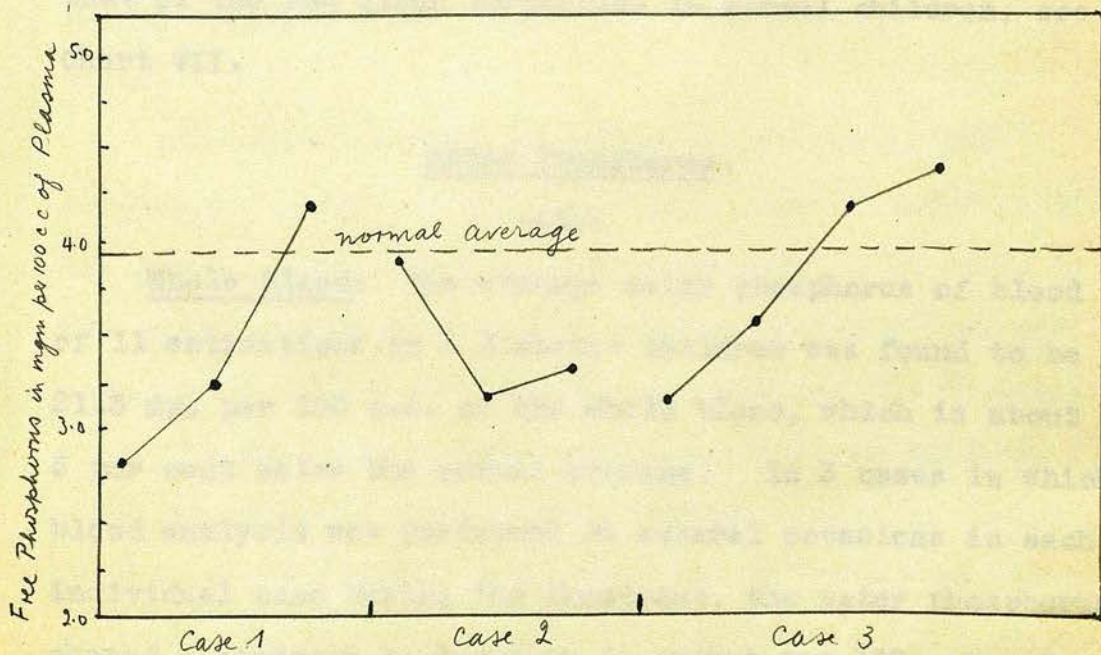
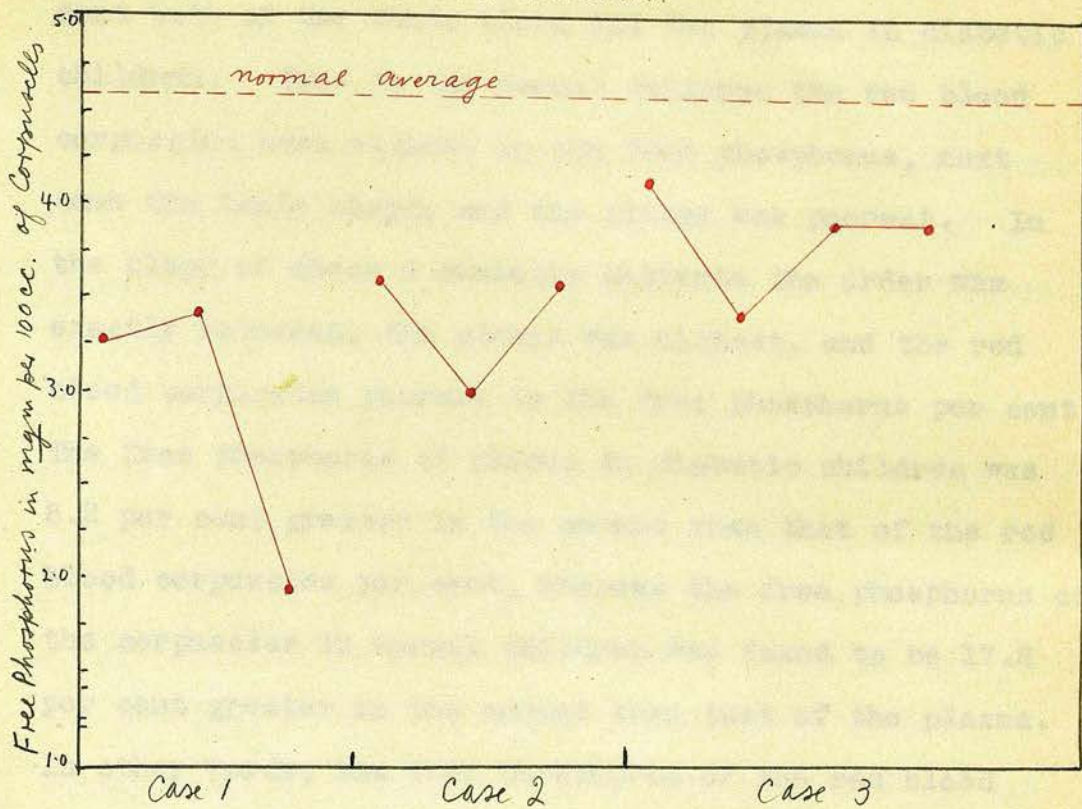
The average free phosphorus of 11 estimations of plasma in 4 diabetic children was found to be 2.3 per cent higher than the average free phosphorus of whole blood. This in itself was not much of a difference, but it gains substantially in significance when it is remembered that the average free phosphorus of the whole blood is 5.6 per cent greater than the average free phosphorus of the plasma in the normal child.

Red Blood Corpuscles: The average free phosphorus of 11 estimations of blood in 4 diabetic children was calculated to be 3.44 mg. per 100 c.c. of the red blood corpuscles. This is 25.7 per cent below the normal average in children. The free phosphorus of the red blood corpuscles evidently suffered most marked change of them all. The lowest observation encountered was only 1.9 mg. of the free phosphorus per 100 c.c. of the red blood corpuscles. This poverty of the red blood corpuscles in the free phosphorus in diabetic children was very striking, because not only did it exist in comparison to that of the corpuscles in the normal children, but it also existed in/



# Chart VII

Distribution of Free Phosphorus of Blood in cases of Diabetes Mellitus.





in relation to the amount of the free phosphorus per cent both of the whole blood and the plasma in diabetic children. Thus in the normal children the red blood corpuscles were richest in the free phosphorus, next came the whole blood, and the plasma was poorest. In the blood of these 4 diabetic patients the order was exactly reversed, the plasma was richest, and the red blood corpuscles poorest in the free phosphorus per cent. The free phosphorus of plasma in diabetic children was 5.2 per cent greater in the amount than that of the red blood corpuscles per cent, whereas the free phosphorus of the corpuscles in normal children was found to be 17.8 per cent greater in the amount than that of the plasma. In other words, the free phosphorus of the red blood corpuscles in diabetic children was very much lower than that of the red blood corpuscles in normal children, see Chart VII.

#### Ester Phosphorus.

-oOo-

Whole Blood: The average ester phosphorus of blood of 11 estimations in 4 diabetic children was found to be 21.3 mg. per 100 c.c. of the whole blood, which is about 5 per cent below the normal average. In 3 cases in which blood analysis was performed on several occasions in each individual case during the treatment, the ester phosphorus showed a tendency to decrease in amount per 100 c.c. of the/

the whole blood. Thus in cases 1, 2, and 3 it dropped from 21.4 to 18.7; 20.2 to 18.13; and 25.22 to 19.95 mg. per 100 c.c. of the whole blood respectively.

Plasma: The average ester phosphorus of the plasma in 11 estimations was found to be within the limits of normality. In the individual cases it showed a tendency to fluctuate appreciably. See Chart VIII.

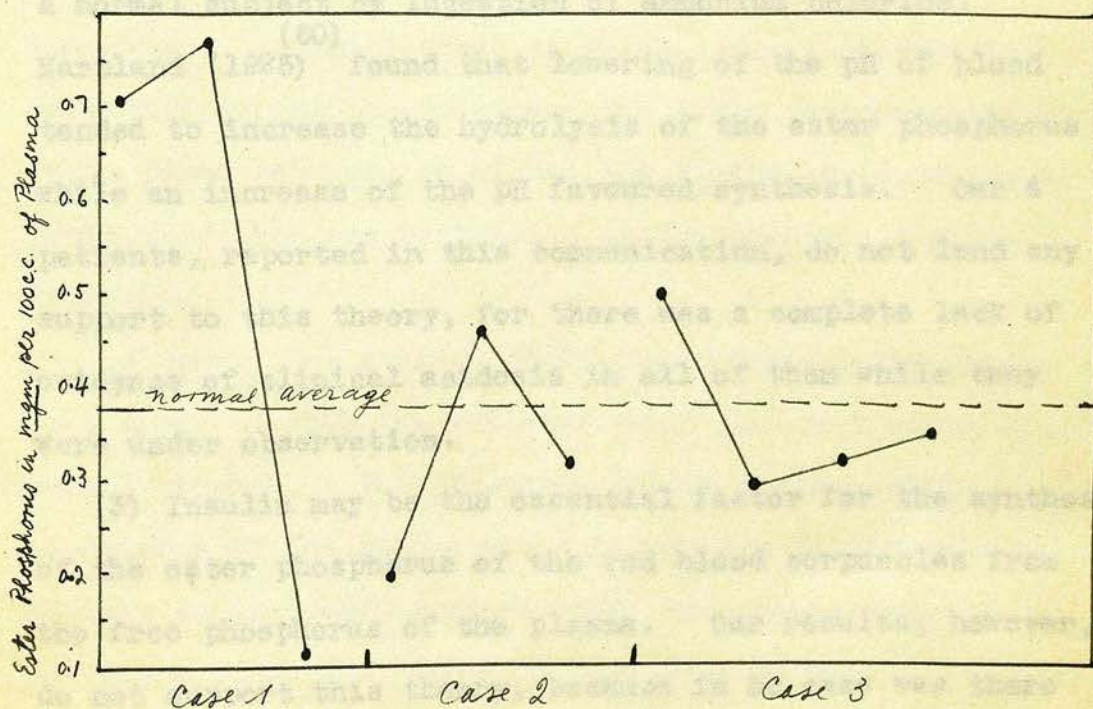
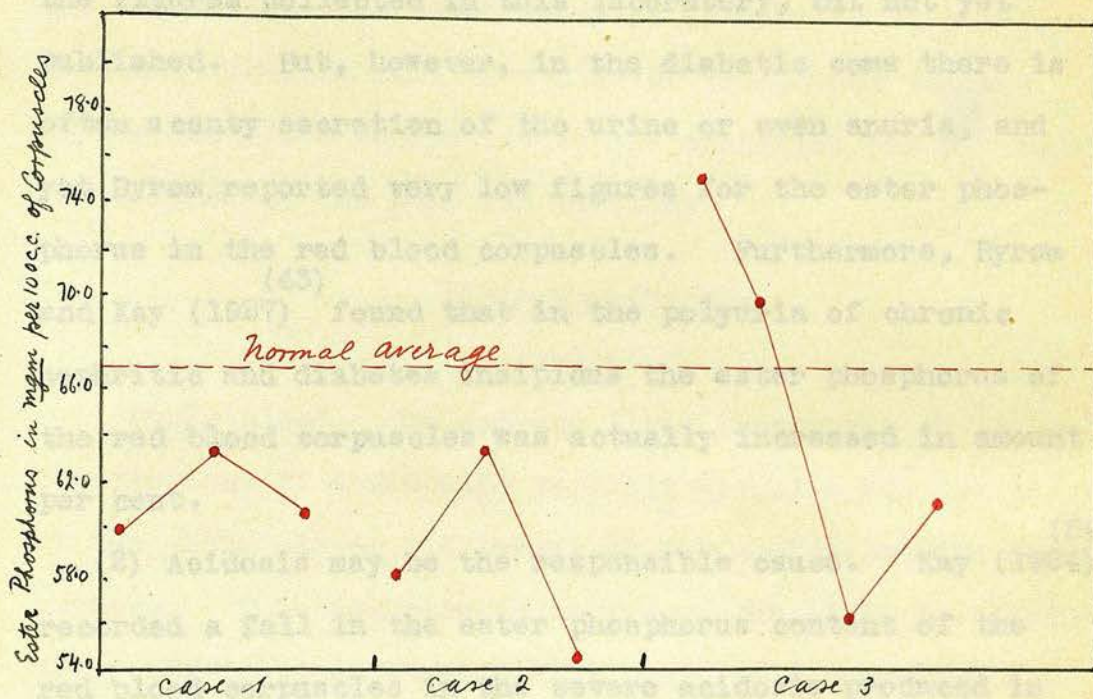
Red Blood Corpuscles: The average ester phosphorus of the red blood corpuscles or the so-called "phosphorus index" of the blood in 11 observations was 61.3 mg. per cent. This is 8.8 per cent below the normal average. (58)  
Byrom (1929) found a definite fall in the ester phosphorus per 100 c.c. of the red blood corpuscles in diabetic patients and in diabetic coma to less than half of the normal. Even though our diabetic patients were not severe examples they supported his contention. See Chart VIII.

This diminution in the ester phosphorus of the corpuscles in the patients suffering from diabetes mellitus has not yet been explained satisfactorily. It might be due to various causes; and it is more probable than not that more than one cause is responsible for the process:

(1) It may be accounted for by polyuria of diabetes mellitus, where it is possible that an excessive amount of the free phosphate is excreted by the kidney as waste product, the ester phosphorus of the red blood corpuscles being/

# Chart VIII

Distribution of Ester Phosphorus of Blood in cases of Diabetes Mellitus





being then drawn upon by the process of hydrolysis to meet the existing deficit. This theory is well supported by the figures collected in this laboratory, but not yet published. But, however, in the diabetic coma there is often scanty secretion of the urine or even anuria, and yet Byrom reported very low figures for the ester phosphorus in the red blood corpuscles. Furthermore, Byrom<sup>(43)</sup> and Kay (1927) found that in the polyuria of chronic nephritic and diabetes insipidus the ester phosphorus of the red blood corpuscles was actually increased in amount per cent.

(2) Acidosis may be the responsible cause. Kay<sup>(59)</sup> (1924) recorded a fall in the ester phosphorus content of the red blood corpuscles in the severe acidosis produced in a normal subject by ingestion of ammonium chloride. Martland<sup>(60)</sup> (1925) found that lowering of the pH of blood tended to increase the hydrolysis of the ester phosphorus while an increase of the pH favoured synthesis. Our 4 patients, reported in this communication, do not lend any support to this theory, for there was a complete lack of evidence of clinical acidosis in all of them while they were under observation.

(3) Insulin may be the essential factor for the synthesis of the ester phosphorus of the red blood corpuscles from the free phosphorus of the plasma. Our results, however, do not support this theory, because in no case was there recorded any increase in amount of the ester phosphorus of/



of the red blood corpuscles. On the contrary, case 3, which was incidentally the most marked diabetic of them all, requiring from 50-60 units of insulin in 24 hours, showed a distinct fall in the ester phosphorus content of the red blood corpuscles as the condition was put under the control by the diet and insulin.

### Lipin Phosphorus.

-oOo-

Whole Blood: The average lipin phosphorus of 11 observations in 4 diabetic patients was 11.5 mg. per 100 c.c. of the whole blood, i.e. about 15 per cent below the normal average. This decrease in amount of the lipin phosphorus of the whole blood was striking especially as case 2 had lipaemia on every occasion the blood was submitted to analysis. In the 3 cases in which several observations were made during the treatment the lipin phosphorus of the whole blood returned to within the limits of normality as their condition was controlled by the diet and insulin therapy.

Plasma: The average lipin phosphorus of the plasma in 4 cases of diabetes mellitus was 7 per cent above the normal average. This increase in the average lipin phosphorus of the plasma was entirely due to lipaemia being present in one patient whose blood was examined on 3 different occasions, and each time yielded very high values for the lipin phosphorus of the plasma. If the values of the blood of this case were excluded the lipin phosphorus of/



of the plasma for the other 3 cases would be just a little below the normal average. See Chart IX.

Red Blood Corpuscles: The average lipin phosphorus of the red blood corpuscles was 14.93 mg. per cent for the 11 estimations in 4 diabetic patients. This amount is actually 35.8 per cent below the normal average. The lowest value recorded was 7.35 mg. per 100 c.c. of the red blood corpuscles. See Chart IX.

(61)  
Bloor (1916) found that the lipoids of the blood in severe diabetes were markedly increased, up to 100 per cent or even more of the normal value. In the cases of mild diabetes mellitus he found the lipoids to be normal. His findings were confirmed later by Byrom. Our results not only failed to confirm their findings, but they showed a very marked poverty of the red blood corpuscles in the lipin phosphorus. The fact that in 3 out of 4 patients the diabetic state was very mild only emphasizes this difference.

Now, taking the individual cases separately, it was noticeable that in each one there was a tendency for the lipin phosphorus of the red blood corpuscles to augment in the amount as the condition was put under the control of insulin, but only in one of them did the content reach the normal level. See Chart IX.

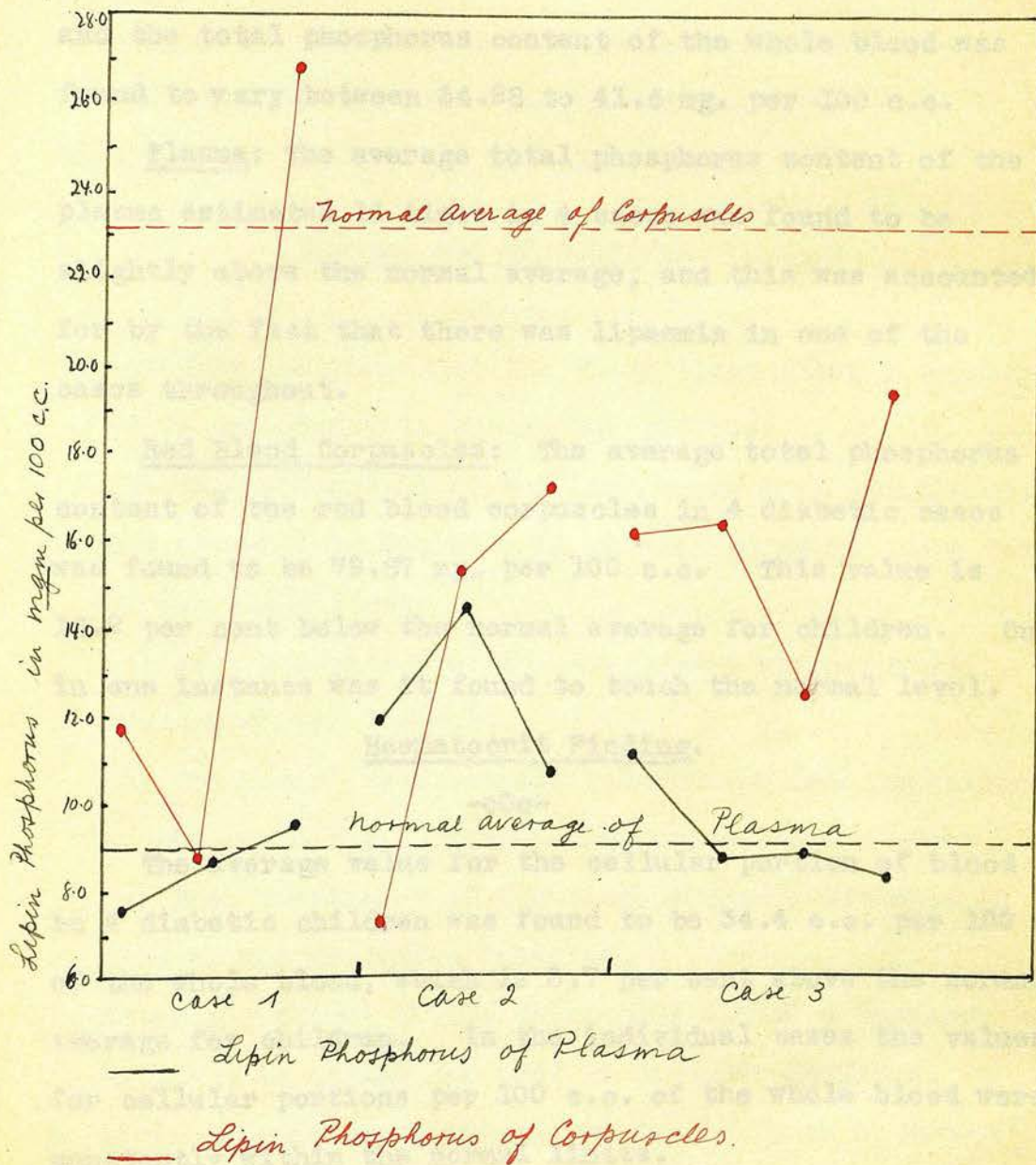
#### Total Phosphorus.

-oOo-

Whole Blood\* The average total phosphorus content of 11 determinations in 4 diabetic patients was found to be 36.34/

# Chart IX

Distribution of the Lipin Phosphorus of Blood in Cases of Diabetes Mellitus





36.34 mg. per 100 c.c. of the whole blood, and this is 9.3 per cent below the normal average. In the individual cases studied on different occasions there was an appreciable variation in amount of the total phosphorus content. Thus, in case 3 the blood was analysed 4 times, and the total phosphorus content of the whole blood was found to vary between 34.28 to 41.6 mg. per 100 c.c.

Plasma: The average total phosphorus content of the plasma estimated 11 times in 4 cases was found to be slightly above the normal average, and this was accounted for by the fact that there was lipaemia in one of the cases throughout.

Red Blood Corpuscles: The average total phosphorus content of the red blood corpuscles in 4 diabetic cases was found to be 79.67 mg. per 100 c.c. This value is 16.2 per cent below the normal average for children. Only in one instance was it found to touch the normal level.

#### Haematocrit Finding.

-oOo-

The average value for the cellular portion of blood in 4 diabetic children was found to be 34.4 c.c. per 100 c.c. of the whole blood, which is 3.7 per cent above the normal average for children. In the individual cases the values for cellular portions per 100 c.c. of the whole blood were constantly within the normal limits.

Calcium/



Calcium Content of the Blood Serum.

-oOo-

The calcium content of the serum was determined independently on 11 different occasions in 4 diabetic cases, and the values were found to vary within the limits of normality. The lowest figure recorded was 9.1 mg. per 100 c.c. of the blood serum, and the highest was 12.3 mg. per 100 c.c. of the blood serum.

Summary and Conclusions.

-oOo-

1. (a) Free phosphorus of the whole blood shows a tendency to be diminished in amount per 100 c.c.  
(b) Free phosphorus of the plasma was also diminished, but showed a tendency to be greater in amount than that of the whole blood.  
(c) Free phosphorus of the corpuscles was markedly diminished per 100 c.c.  
(d) The normal relationship between the free phosphorus of the whole blood, plasma and corpuscles was upset.  
(e) Free phosphorus of the blood showed a tendency to rise as the condition improved.
2. Ester phosphorus of the corpuscles showed a tendency to decrease in amount per cent in diabetes mellitus.
3. Lipin phosphorus of the plasma was not much altered.  
Lipin phosphorus of the red blood corpuscles was markedly diminished in amount. During the treatment it showed a tendency to rise gradually.

4. Total phosphorus content of the whole blood was diminished. Total phosphorus of the plasma was within the limits of normality. Total phosphorus content of the corpuscles was diminished in amount per 100 c.c.
5. Calcium content of the blood serum was found to be within the limits of normality.

Distribution of the Phosphorus Compounds of Blood  
in Infantile Tetany.

-000-

The pathological condition of infantile tetany has been recognized as a clinical entity for many years, and various theories as to its pathogenesis have been put forward. In turn, it has been suggested that it is due (a) to disease of the parathyroid glands, (b) to the character of the food, (c) to intoxication by calcium, (d) to intoxication by gaunidin or methylgaunidin, and (e) to the lack of calcium, but the evidence at present available fails to confirm any one of these theories.

(62)

Howland and Marriott (1918) appeared to be the first workers to describe the characteristic blood chemistry in infantile tetany. They showed that the calcium content of the blood serum was greatly reduced in the active stage of tetany, and that the inorganic phosphate of the blood serum was not "significantly increased" in the amount per cent. Kramer, Tisdall, and Howland (1921) reported on the average normal values for the inorganic phosphate of the serum in 7 cases of infantile tetany. Next, Hess, Colvin, Wang and Fletcher (1923) examined the inorganic phosphate, and the calcium content of the blood serum in 16 cases of active tetany, and they reported that the calcium content of the serum was considerably reduced, but in no instance did they find the inorganic phosphate of the blood serum elevated above the normal level. Hoag (1923)/

(66)  
(1923) in the course of his study on the use of ultra-violet light in the treatment of tetany, analysed the blood serum for calcium and inorganic phosphate in 11 cases two of which showed values for the inorganic phosphate above the normal level. Scott and Usher  
(65)  
(1926) analysed the blood serum of 21 infants with active tetany for the inorganic phosphate, and they found high figures only in 2 cases. Marples and Crump (1930)<sup>(67)</sup> examined the blood serum for the inorganic phosphate in a series of 80 cases of tetany, 20 of which (25%) showed an increase in amount of about 21 per cent in the inorganic phosphate of the blood serum. They failed to observe any clinical characteristics which might differentiate the group of cases with the high concentration of the inorganic phosphate of the blood serum from those with the normal or low inorganic phosphate values of the blood serum.

The inorganic phosphate has been reported to vary in infantile tetany, but there appears to be a great deal of confusion regarding the infantile tetany complicated with rickets, and the infantile tetany without rickets.

#### Author's Results.

-c0o-

As it is well known that the phosphorus plays an important role in the process of ossification of the bones, and, still further, that the inorganic phosphate is only about/



about  $\frac{1}{10}$  part of the total phosphorus content of the blood this opportunity was taken to carry out complete analysis of the phosphorus compounds of the blood in 5 cases of active tetany, and study their relative distribution between the plasma and red blood corpuscles. In so far as the author is aware no similar work has been published on the partition of all the phosphorus compounds of blood in infantile tetany. The results appear in Table VI.

#### Free Phosphorus.

-c0o-

Whole Blood: The average free phosphorus in 5 cases of active tetany was found to be 4.97 mg. per 100 c.c. of the whole blood. This is about 20 per cent above the normal average for children. In 3 out of 5 cases (60%) the free phosphorus rose markedly above the normal level. In the other 2 the free phosphorus did not rise above the normal level.

Plasma: The free phosphorus values for the blood plasma in 5 cases of tetany showed the same tendency as those for the whole blood.

Red Blood Corpuscles: The free phosphorus of the red blood corpuscles preserved its proportionate values to those of the plasma and whole blood tetany.

Table VI.

Results of the Phosphorus Compounds of Blood in Infantile Tetany.

Name and Age	Whole Blood						Plasma						Corpuscles				Haema- tocrit RBCs%	Ca. Serum.	
	F.P.	F.E.P.	E.P.	L.P.	Comb T.P.	Add. T.P.	F.P.	F.E.P.	E.P.	L.P.	T.P.	F.P.	L.P.	E.P.	T.P.				
		mgm. per 100 c.c.						mgm. per 100 c.c.						mgm. per 100 c.c.					
Normal Average	4.15	26.36	22.4	13.74	40.2	40.11	3.93	4.31	0.38	9.06	13.12	4.63	23.26	67.25	95.13	33.15	10.73		
15 J.K. aet 1½ yrs	5.5	22.9	17.35	8.0	31.2	30.9	5.4	5.53	0.13	4.06	9.59	5.9	18.2	61.6	85.7	28.0	8.1		
16 J.M. aet 4½ yrs	3.5	23.4	19.9	10.4	33.4	33.8	3.22	3.36	0.14	6.39	9.75	4.15	19.4	64.2	87.75	30.8	5.2		
17 J.C. aet 1½ yrs	4.04	25.2	21.16	11.7	37.4	36.9	3.89	4.5	0.61	6.0	10.5	4.34	23.0	62.1	89.44	33.4	5.3		
18 T.M. aet 3½ yrs	5.74	27.1	21.36	10.4	36.7	37.5	5.2	5.45	0.25	9.47	14.92	7.1	12.7	74.9	94.7	28.4	4.8		
19 G.T. aet 1½ yrs	6.1	33.4	27.3	9.26	42.73	42.66	6.17	6.58	0.41	6.48	12.65	6.0	13.7	70.3	90.0	38.5	5.2		
Average	4.97	26.4	21.41	9.95	36.28	36.23	4.75	5.08	0.3	6.48	11.48	5.5	17.4	66.6	89.52	31.8	5.72		

F.P. = Free Phosphorus: F.E.P. = Free plus Ester Phosphorus: L.P. = Lipin Phosphorus:

T.P. = Total Phosphorus.

Ester Phosphorus.

-oOo-

Whole Blood: The average ester phosphorus of the whole blood in 5 cases of infantile tetany was found to be 21.4 mg. per 100 c.c. which is 4.4 per cent below the normal average. In 4 cases the ester phosphorus was diminished appreciably, and only in one case was it increased markedly.

Plasma: The average ester phosphorus of the plasma was found to be 21 per cent below the normal average. The lowest figure recorded was 0.13 mg. and the highest 0.61 mg. per 100 c.c. of the plasma.

Red Blood Corpuscles: The average ester phosphorus of the red blood corpuscles in 5 cases of tetany was found to be 66.6 mg. per 100 c.c., which is less than 1 per cent below the normal level. In each individual case the ester phosphorus of the red blood corpuscles was within the limits of normality.

Lipin Phosphorus.

-oOo-

Whole Blood: The average lipin phosphorus of the whole blood in 5 cases of tetany was found to be 9.95 mg. per cent, which is 27.5 per cent below the normal average. The lipin phosphorus of the whole blood was found uniformly diminished in each individual case.

Plasma: The average lipin phosphorus of the plasma was/

was found to be 6.48 mg. per cent, or 28.4 per cent below the normal average. In one case it was as low as 4.06 mg. per 100 c.c. of the plasma - a decrease of 55 per cent below the normal average. Only in one case was it found within the limits of normality.

Red Blood Corpuscles: The average lipin phosphorus of the red blood corpuscles in 5 cases of tetany was 17.4 mg. per 100 c.c., i.e. 25 per cent below the normal average. In 4 of the 5 cases it was appreciably diminished, in one amounting to 50 per cent. In the remaining one it was within the limits of normality.

#### Total Phosphorus.

-oOo-

Whole Blood: The average total phosphorus content of the whole blood in 5 cases of tetany was 36.23 mg. per 100 c.c., which is 9.6 per cent below the normal average. In 4 out of 5 cases the total phosphorus content was appreciably diminished, the lowest figure recorded being about 23 per cent below the normal average. In the remaining case it was slightly above the normal average.

Plasma: The average total phosphorus content of the plasma in 5 cases of tetany was 11.48 mg. per 100 c.c., which is 12.5 per cent below the normal average. In 4 out of 5 cases the total phosphorus content was appreciably decreased in amount, the lowest figure being about 20 per cent below the normal average. In the other case



the total phosphorus content was within the limits of normality.

Red Blood Corpuscles: The average total phosphorus of the red blood corpuscles in 5 cases was 89.52 mg. per 100 c.c., which is 5.9 per cent below the normal average. There was no great variation between individual cases.

#### Haematocrit Finding.

-oOo-

The average cellular portion of the whole blood in 5 observations was 31.8 cc. per 100 c.c. of the whole blood which is 4 per cent below the average normal.

#### Calcium Content of the Blood Serum.

-oOo-

Calcium content of the blood serum was determined independently in each individual case, and very low values were found. The highest figure recorded was 8.1 mg. per 100 c.c. of the blood serum. All the other figures were below 6 mg. per 100 c.c. of the blood serum.

-----

Distribution of Calcium of the Blood in Infantile  
in Infantile Tetany.

-oOo-

The question of the presence of calcium in the red blood corpuscles has often been a subject of considerable discussion.

(68)  
Hamburger (1909) reported as much as 32 mg. of calcium per 100 c.c. of red blood corpuscles. Cowie and (69)  
Colhoun (1919) also found an average of 4.26 mg. of the calcium per 100 c.c. of unwashed human red blood corpuscles, and 3.47 mg. per 100 c.c. of washed red blood corpuscles. (18)  
Jones and Nye (1921) also insisted upon the presence of calcium in the red blood corpuscles in appreciable amounts, their average being 8.7 mg. per 100 c.c. red blood cor- (70)  
puscles. Jones (1921) also obtained an average calcium of 5 mg. per 100 c.c. of red blood corpuscles in the new (30)  
born. Anderson (1924) reported figures from 3.1 to 5.5 mg. of calcium per 100 c.c. of the red blood corpuscles, and (71)  
Stanford and Wheatley (1925) claimed that the human red blood corpuscles contain from 1.4 to 3 mg. of calcium per 100 c.c.

(72)

On the other hand, as early as 1898 Abderhalden in a study of the substances of the blood in various animals such as the cow, bull, sheep, horse, pig, rabbit, dog, and the cat, never found any calcium in the red blood corpuscles.

(73)

(74)

Richter-Quittner (1921) and Falta (1921) also failed to

find/

find calcium present either in the human red blood corpuscles or in those of the animal which they investigated. Kramer and Tisdall (1922)<sup>(75)</sup> also stated that the red blood corpuscles of human blood did not contain appreciable amounts of calcium. Stewart and Percival (1928)<sup>(76)</sup> failed to demonstrate more than a mere trace (from 0.15 to 0.30 mg. per 100 c.c. of corpuscles) of the calcium in the corpuscles. Leiboff (1930)<sup>(77)</sup> found no calcium in the human red blood corpuscles.

#### Author's Results.

-oOo-

The calcium content was determined directly both in the whole blood, and the plasma, and then by means of calculations the figures for the red blood corpuscles were obtained.

#### Methods:

Determinations of the calcium content of the plasma were made according to the method described by Kramer and Tisdall (1921)<sup>(78)</sup>.

(2) Determinations of the calcium content in the whole blood were made by the method described by Anderson (1924)<sup>(30)</sup>.

(3) Haematocrit readings were taken from the oxalated blood spun in a centrifuge for about 40-45 minutes at the rate of 3000 revolutions per minute.

Normal/

Normal Blood.

-oOo-

Calcium content was determined in the whole blood, and the serum of 5 normal children, and the calculated results for the red blood corpuscles are given in Table VII.

In Table VII showing the findings regarding calcium content of the red blood corpuscles (determined by calculation) it will be seen that they are in agreement with those of the later workers who found that corpuscles contain practically no calcium.

Blood of the Cases suffering from Active Tetany.

-oOo-

Calcium content of the whole blood, and the plasma in 2 cases of infantile tetany was determined directly, and the calculated values for the red blood corpuscles are given in Table VIII.

The red blood corpuscles of the blood in infantile tetany complicated with rickets contained an appreciable amount of calcium per 100 c.c.

Summary and Conclusions.

-oOo-

1. Free phosphorus of the whole blood, the plasma, and the red blood corpuscles showed a tendency to rise appreciably in 60% of our cases.



Table VII.

Distribution of Calcium in Normal Children.

No.	Name	Calcium in mgm. per 100c.c. of Blood Serum	Calcium in mgm. per 100c.c. of Whole Blood	Calcium in mgm. per 100c.c. of Corpuscles.
1.	C.G.	10.2	6.82	0.3
2.	J. McE.	9.72	6.99	0.31
3.	E.C.	10.9	7.52	0.
4.	A.M.	11.1	7.1	0.27
5.	A.G.	11.4	6.99	0.05

Table VIII.

Distribution of Calcium in Infantile tetany.

No.	Name	Calcium in mgm. per 100c.c. of Blood Serum	Calcium in mgm. per 100c.c. of Whole Blood	Calcium in mgm. per 100c.c. of Corpuscles.
1.	J.L.	7.1	5.56	1.34
2.	G.T.	5.2	3.7	1.3

2. (a) The ester phosphorus of the whole blood showed a tendency to fall appreciably.
- (b) The ester phosphorus of the plasma was below the normal level.
- (c) There was no appreciable change in the ester phosphorus of the red blood corpuscles.
3. The lipin phosphorus of the whole blood, the plasma, and the red blood corpuscles was markedly diminished per cent.
4. The total phosphorus content of the whole blood, plasma, and the red blood corpuscles showed a tendency to diminish in amount per cent.
5. The calcium content of the blood serum in tetany is considerably diminished.
- The red blood corpuscles of the blood in normal children are devoid of calcium.
6. The red blood corpuscles of the blood in tetany contain an appreciable amount of the calcium per 100 c.c.

#### ----- Conclusions.

We have studied the partition of the phosphorus compounds of the blood in examples of idiopathic hypoparathyroidism, secondary anemia, rickets, etc. Though the results for any particular disease are too scanty to warrant definite conclusions yet they indicate some

Miscellaneous Group.

-oOo-

Comparatively few data are available on the complete distribution of the phosphorus compounds of the blood in pathological conditions other than those already discussed. <sup>(79)</sup>McGlusky (1925) published his work on the distribution of the phosphorus compounds of the blood in tuberculosis. He reported that the inorganic phosphate of the blood plasma in tuberculosis was higher in concentration than in the normal subjects. <sup>(80)</sup>Roller (1926) studied the phosphorus compounds of the blood in the cases of numerous diseases such as pneumonia, neuresthenia, chronic bronchitis, etc., and he found a moderate, though inconclusive, variation in the partition of the phosphorus compounds in the blood. <sup>(81)</sup>Byrom and Kay (1928) also studied the distribution of the phosphorus compounds of the blood in anaemia, polycythaemia, and leukaemia: to this work reference will be made later.

Author's Findings.

-oOo-

We have studied the partition of the phosphorus compounds of the blood in examples of idiopathic convulsions, secondary anaemia, rickets, etc. Though the results for any particular disease are too scanty to warrant definite conclusions yet they indicate some interesting/

**TABLE IX - Results of the Phosphorus compounds in blood  
of miscellaneous cases.**

Name & Age	Diagnosis	W H O L E B L O O D.							P L A S M A					C O R P U S C L E S				Haema- tocrit R.B.CS%	Ca. Serum mgm%
		F.P.	F.E.P.	E.P.	L.P.	Comb.	add.	F.P.	F.E.P.	E.P.	L.P.	T.P.	F.P.	L.P.	E.P.	T.P.			
						T.P.	cc.										mgm per 100		
Normal Average		4.15	26.36	22.4	13.74	40.2	40.11	3.93	4.31	0.38	9.06	13.12	4.63	23.26	67.25	95.13	33.15	10.73	
21.B.R. $\frac{4}{52}$ yr.	Idiop Con- vulsions	6.49	25.3	18.81	11.41	36.7	36.76	5.79	6.25	0.46	7.35	13.6	8.5	23.3	72.7	104.5	25.4	-	
22.G.K. $\frac{5}{52}$ yr.	do do	5.37	23.1	17.73	9.8	33.3	32.9	5.3	5.9	0.6	5.18	11.08	5.5	21.8	62.2	89.5	27.8	-	
23.R.A. 12 "	Sec. Anaemia	4.52	23.5	18.98	10.07	33.6	33.51	4.3	4.45	0.15	8.15	12.6	5.2	16.5	81.3	103.0	23.2	10.8	
24.L.A. 6 $\frac{11}{12}$ "	" "	3.98	23.6	19.62	10.3	34.2	33.9	3.8	4.1	0.3	8.4	12.5	4.6	16.1	79.5	100.2	24.4	10.9	
25.D.McS. 8 "	" "	4.1	25.3	21.2	11.2	36.17	36.5	3.8	4.2	0.4	9.1	13.1	4.87	16.6	74.9	96.37	27.9	9.12.	
26.M.T. 3 $\frac{1}{2}$ "	Purpura Simplex	3.25	20.61	17.36	9.05	30.4	29.66	3.32	3.7	0.38	7.2	10.52	3.07	13.7	60.3	77.1	28.3	11.06	
27.W.M. 6 $\frac{1}{2}$ "	Ununited fracture of Tibia	6.1	29.2	23.1	13.2	43.8	42.4	5.13	8.2	3.07	5.4	13.6	7.9	28.1	61.1	97.1	34.5	11.1	
28.J.W. 1 $\frac{5}{12}$ "	Rickets	3.21	23.84	20.63	12.07	36.43	35.91	3.32	3.52	0.2	8.55	12.07.	2.9	19.6	64.6	87.1	31.7	8.14	
29.D.M. 5 $\frac{1}{2}$ "	Albuminuria	4.87	25.9	21.3	10.22	36.23	36.12	5.57	6.06	0.49	9.81	15.87	3.6	10.9	57.8	71.6	36.3	-	
30.M.H. 8 "	Lymphad- enonia	4.06	23.89	19.83	11.74	36.13	35.63	4.2	4.56	0.36	6.08	10.69	3.79	22.6	57.1	83.49	34.3	9.8	
31.C.G. 9 $\frac{1}{2}$ "	Dwarf.	4.36	29.2	24.84	9.8	39.13	39.0	4.03	4.7	0.67	7.76	12.46	5.0	13.9	73.4	92.3	33.2	9.91	

F.P. - Free phosphorus; F.E.P. - Free plus este phosphorus; L.P. Lipin phosphorus; T.P. - Total phosphorus.



interesting changes in the partition of the phosphorus compounds of the blood and it was considered justifiable to include them here. The results appear in Table IX.

In order to avoid unnecessary complications it is proposed to take up the results of each different disease in order, and treat them separately.

#### 1. Idiopathic Convulsions.

-oOo-

There were only two cases of idiopathic convulsions available for the study. They were  $\frac{4}{52}$  yr. and  $\frac{5}{52}$  yr. old respectively. From their histories and physical examinations no apparent cause was found to account for the condition. Lumbar puncture was performed in both of them, and the cerebro-spinal fluid was found devoid of any abnormal changes.

The blood was submitted to analysis for the phosphorus compounds and the following changes in the partition of the phosphorus compounds of the blood were observed.

#### Free Phosphorus.

-oOo-

Whole Blood: The average free phosphorus of the blood was found to be 5.93 mg. per 100 c.c. of the whole blood, which is 42 per cent above the normal average. In both cases the free phosphorus fraction was markedly increased.

Plasma/

Plasma: The average free phosphorus of the plasma in 2 cases of idiopathic convulsions was 5.54 mg. per 100 c.c., 41 per cent higher than the normal average. This increase in the free phosphorus was recorded in both cases independently.

Red Blood Corpuscles: The average free phosphorus of the red blood corpuscles in 2 cases was 7.0 mg. per 100 c.c., which is 51 per cent above the normal level. The rise in the inorganic phosphorus was observed in both cases independently.

Young infants might give slightly higher values for the free phosphorus of the blood, but in this instance the values were too high to be accounted for satisfactorily by that factor, and the cause probably lay elsewhere. Conceivably kidneys might be incriminated to be defective in the power to excrete inorganic phosphates, but clinically there was nothing even to suggest such a possibility though the free phosphorus of the urine was not estimated.

#### Ester Phosphorus.

-oCo-

Whole Blood: The average ester phosphorus of the blood in 2 cases was 18.27 mg. per 100 c.c., which is 18.4 per cent below the normal average. It was diminished in both cases.

Plasma: The average ester phosphorus of the plasma was/

was 0.53 mg. per 100 c.c. which is about 40 per cent above the normal average. The plasma of both individual cases rose in concentration above the normal level.

Red Blood Corpuscles: The average of the ester phosphorus of the red blood corpuscles in 2 cases was 67.4 mg. per 100 c.c. Both the average and the values for individual cases were within the limits of normality.

#### Lipin Phosphorus.

-c0o-

Whole Blood: The average lipin phosphorus of the whole blood in 2 cases was 10.6 mg. per 100 c.c., which is 22.8 per cent below the normal average. It was diminished in amount in both cases independently.

Plasma: The average lipin phosphorus of the plasma was 6.26 mg. per 100 c.c., and this is 30.8 per cent below the normal average. The plasma of both cases showed diminution in the lipin phosphorus per 100 c.c.

Red Blood Corpuscles: The average lipin phosphorus of the red blood corpuscles was found to be 22.5 mg. per 100 c.c., which is within the limits of normality.

#### Total Phosphorus.

-c0o-

Whole Blood: The average amount of the total phosphorus of the whole blood was 34.83 mg. per 100 c.c., which is 13.1 per cent below the normal average. This fall in amount of the total phosphorus was noted in both cases/

cases independently.

Plasma: The average amount of the total phosphorus of the plasma was 12.34 mg. per 100 c.c., which is 5.9 per cent below the normal average.

Red Blood Corpuscles: The average total phosphorus content of the red blood corpuscles in 2 cases was 97.0 mg. per 100 c.c., which is about 2 per cent above the normal average.

#### Haematocrit Finding.

-cCo-

The cellular portion of the whole blood was found diminished in amount per 100 c.c. in both cases. The average value for the 2 cases is 19.7 per cent below the normal average value.

#### Summary and Conclusions.

1. Free phosphorus of the blood in 2 cases of idiopathic convulsions showed a tendency to rise considerably in amount per 100 c.c.
2. (a) ester phosphorus of the whole blood was decreased in amount.  
(b) Ester phosphorus of the plasma was increased.  
(c) Ester phosphorus of the red blood corpuscles was normal in amount per 100 c.c.
3. The lipin phosphorus of the whole blood and the plasma was markedly diminished per 100 c.c., but the lipin phosphorus of the red blood corpuscles was normal.



4. The total phosphorus of the whole blood showed a tendency to decrease in amount per 100 c.c. The total phosphorus of the plasma was slightly decreased, and that of the red blood corpuscles was normal.

-----

## 2. Secondary Anaemia.

-c0o-

Three examples of this condition were examined. In 2 of the 3 cases no other pathological evidence was present to account for the anaemic state except some carious teeth. In the remaining case the condition was present in a child recovering from rheumatic fever.

The blood was analysed completely for the distribution of the phosphorus compounds of the blood in every one of them, and the following results were obtained.

### Free Phosphorus.

-c0o-

The average free phosphorus of the whole blood, plasma, and the red blood corpuscles remained within the limits of normality. In each individual case the variation was normal.

### Ester Phosphorus.

-c0o-

Whole Blood: The average ester phosphorus of the whole blood was found to be 19.7 mg. per 100 c.c., which

is 12 per cent below the normal average. In each individual case the ester phosphorus content of the whole blood per cent was invariably diminished.

Plasma: The average ester phosphorus of the plasma was 0.28 mg. per 100 c.c., which is 26.3 per cent below the normal average.

Red Blood Corpuscles: The average ester phosphorus of the red blood corpuscles was 78.6 mg. per 100 c.c., an increase of about 17 per cent above the normal average. In each individual case the value for the ester phosphorus of the red blood corpuscles was appreciably higher than the normal average. This invariable increase in the ester phosphorus was in agreement with what one might expect if there were an increased proportion of the young cells in blood whose ester phosphorus content is generally admitted to be slightly above the normal. Further, these values for the ester phosphorus of the red blood corpuscles in secondary anaemia confirmed the findings for the same condition published by Byrom and Kay (1928)<sup>(87)</sup>

#### Lipin Phosphorus.

-000-

Whole Blood: The average lipin phosphorus of the whole blood in 3 cases of secondary anaemia was 10.5 mg. per 100 c.c., a decrease of 23.5 per cent below the normal average. This decrease in value was present in all 3 cases separately.

Plasma/

Plasma: The average lipin phosphorus of the plasma was 8.55 mg. per 100 c.c., a decrease of 5.5 per cent below the normal level.

Red Blood Corpuscles: The average lipin phosphorus of the red blood corpuscles was 16.4 mg. per 100 c.c., i.e. 29 per cent below the normal level. This low value for the lipin phosphorus was uniform in all the cases.

(82)

Bloor and Macpherson (1917) while studying lipoids in anaemia were led to conclude that the blood lipid values in anaemia were normal as long as the percentage of the red blood corpuscles remained above half the normal value. When the percentage was below this level the abnormalities began to appear which, in the order of their magnitude and also of the frequency of their occurrence were:-

- (1) High fat in the plasma.
- (2) Low cholesterol in the plasma, and occasionally in the corpuscles, and
- (3) Low lecithin in the plasma.

They also found that the lipid composition of the corpuscles was normal in almost all the cases. The figures of our cases for lipin phosphorus of the red cells do not support their conclusions.

(83)

Bloor (1920-21) studied rabbits in which lipaemia was produced by the acute experimental anaemia through haemorrhage, and he showed that of all the phosphoric acid compounds of the blood, the lipid phosphorus was most/

most markedly affected by the anaemia and subsequent lipaemia. Values up to 5 times the normal were found in the plasma, and 2 times or over the normal in the red blood corpuscles. When the lipoid phosphorus was markedly above the normal there was an increase in the inorganic phosphate. Organic phosphorus of the corpuscles on the other hand remained remarkably constant throughout the experiments. Organic phosphorus of the plasma, however, varied greatly. They concluded that the only phosphorus which was notably higher in the newly formed red blood corpuscles than in the older ones was the lipoid phosphorus. Our results for the lipin phosphorus in 3 cases of secondary anaemia showed a tendency to be slightly diminished in the plasma and markedly so in the red blood corpuscles which state was in absolute contradiction to his findings, but this discrepancy might be due to the fact that their results were obtained from rabbits after experimental anaemia followed by lipaemia, and ours were obtained from the blood of the patients suffering from secondary anaemia with no evidence of lipaemia.

(81)

Byrom and Kay (1928) contended that in secondary anaemia the individual cases varied somewhat in their phosphorus partition, but the average figures showed that, on the whole, the changes in the phosphorus partition were due merely to the change in the relative proportion/



proportion of the red blood corpuscles and plasma and were not due to any qualitative change in the nature of their phosphorus compounds. As they appeared to have estimated only the phosphorus compounds of the whole blood it was very easy to arrive at somewhat deceptive conclusions. For instance, if the relative diminution of the cellular portion of the blood in secondary anaemia is seldom so very marked, and as the plasma contains an appreciable amount of the lipin phosphorus, there can not be expected more than a slight diminution in the lipin phosphorus per 100 c.c. of the whole blood. But if this slight diminution in the lipin phosphorus of the whole blood is directly at the expense of the red blood corpuscles, and the latter are relatively diminished per 100 c.c. of whole blood, it is evident that the fall in the lipin phosphorus will be much greater per 100 c.c. of the red blood corpuscles, and this our results confirm.

#### Haematocrit Finding.

-oOo-

The average cellular portion of the blood in 3 cases of secondary anaemia was 25.1 c.c. per 100 c.c. of the whole blood, a decrease of 24.2 per cent below the normal average. The decrease in the cellular portion per 100 c.c. of the whole blood was marked in all the cases.

Calcium/

Calcium Content of the Blood Serum.

-oOo-

The calcium content of the blood serum in 3 cases of secondary anaemia was determined, and found to be within the limits of normality.

Summary and Conclusions.

-oOo-

1. Free phosphorus of the blood was within normal limits.
2. Ester phosphorus of the whole blood and the plasma showed a tendency to fall appreciably in the amount.
3. Ester phosphorus of the red blood corpuscles was increased.
4. Lipin phosphorus of the whole blood showed a tendency to fall appreciably, that of the red blood corpuscles markedly, and that of the plasma was within normal limits.
5. Calcium content of the blood plasma was normal.

3. Purpura Simplex.

-oOo-

Only one case of purpura simplex was available for the purpose of studying the distribution of the phosphorus compounds of the blood, and the following changes were noted.

Free/

Free Phosphorus.

-000-

Whole Blood: The free phosphorus was found to be 3.25 mg. per 100 c.c. of the whole blood, a decrease of 21.9 per cent below the normal level.

Plasma: The free phosphorus of the plasma was 3.32 mg. per 100 c.c., a decrease of 15.5 per cent below the normal level. The free phosphorus of the plasma was slightly higher in concentration than the free phosphorus of the whole blood per 100 c.c., which was the reverse of that of the normal for children.

Red Blood Corpuscles: The free phosphorus of the red blood corpuscles seemed to suffer the greatest loss. It was found to be only 3.07 mg. per 100 c.c., which is 33.6 per cent below the normal level. It was actually smaller in the amount per 100 c.c. than either that of the plasma or the whole blood, whereas in the normal blood it was the highest in amount per 100 c.c.

Ester Phosphorus.

-000-

Whole Blood: The ester phosphorus of the whole blood was 17.36 mg. per 100 c.c., and this is 22.5 per cent below the normal level. This decrease was due chiefly to the relative diminution of the red blood corpuscles of the whole blood.

Plasma: The ester phosphorus of the plasma was 0.38/

0.38 mg. per 100 c.c., which was normal.

Red Blood Corpuscles: The ester phosphorus of the red blood corpuscles was 60.3 mg. per 100 c.c., a decrease of 10.3 per cent below the normal level. The cellular portion of the whole blood appearing smaller in amount per 100 c.c., this finding was rather contrary to what would have been expected had the blood changes been due simply to anaemia.

Lipin Phosphorus.

-oOo-

Whole Blood: The lipin phosphorus of the whole blood was 9.05 mg. per 100 c.c., a marked decrease of 34 per cent below the normal level.

Plasma: The lipin phosphorus of the plasma was 7.2 mg. per 100 c.c., which is 20.5 per cent below the normal average.

Red Blood Corpuscles: The lipin phosphorus of the red blood corpuscles was 13.6 mg. per 100 c.c., and this is 41 per cent lower than the normal average in children.

Total Phosphorus.

-oOo-

Whole Blood: The total phosphorus of the whole blood was only 29.66 mg. per 100 c.c., a decrease of 26 per cent below the normal average.

Plasma: The total phosphorus content of the plasma was 10.52 mg. per 100 c.c., a decrease of 19 per cent below the/



the normal.

Red Blood Corpuscles The total phosphorus of the red blood corpuscles was 77.1 mg. per 100 c.c., which is 19 per cent below the normal average.

Haematocrit Finding.

-oOo-

The amount of the red blood corpuscles was 28.3 c.c. per 100 c.c. of the whole blood, a decrease of 14.8 per cent below the normal.

Calcium Content of the Blood Serum.

-oOo-

Calcium content of the blood serum was 11.06 mg. per 100 c.c.

Summary.

-oOo-

1. There was a general tendency for all the phosphorus compounds to be markedly diminished in amount per 100 c.c. of the whole blood, plasma, and the corpuscles.
2. The normal relationship of the free phosphorus of the whole blood, plasma, and the corpuscles was disturbed, that of the corpuscles being lowest in the amount per 100 c.c.
3. Calcium content of the serum was, if anything, uncreased in amount per 100 c.c.

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Ununited/

#### 4. Ununited Fracture of Tibia.

-oOo-

The patient was born with fracture of left tibia, which has persisted even since notwithstanding two operations and plating of the bones. In view of this interesting history of the condition the analysis of blood for partition of the phosphorus compounds was carried out and the following striking changes were observed.

##### Free Phosphorus.

-oOo-

Whole Blood: The free phosphorus of the whole blood was 6.1 mg. per 100 c.c., an increase of 47 per cent above the normal.

Plasma: The free phosphorus of the plasma was 5.13 mg. per 100 c.c., an increase of 30.5 per cent above the normal.

Red Blood Corpuscles: The free phosphorus of the red blood corpuscles was 7.9 mg. per 100 c.c., an increase of 70.6 per cent above the normal average.

##### Ester Phosphorus.

-oOo-

Whole Blood: The ester phosphorus of the whole blood was 23.1 mg. per 100 c.c., which is 3.1 per cent above the normal.

Plasma: The ester phosphorus of the plasma was 3.07/

3.07 mg. per 100 c.c., or 708 per cent above the normal average. This was a very striking increase, and we found it in no other condition.

Red Blood Corpuscles: The ester phosphorus of the red blood corpuscles was 61.1 mg. per 100 c.c., which is 9 per cent below the normal average.

#### Lipin Phosphorus.

-oOo-

Whole Blood: The lipin phosphorus of the whole blood amounted to 23.1 mg. per 100 c.c., which is only 3.6 per cent below the normal level.

Plasma: The lipin phosphorus of the plasma was only 5.4 mg. per 100 c.c., which is 40.4 per cent below the normal average.

Red Blood Corpuscles: The lipin phosphorus of the red blood corpuscles was 28.1 mg. per 100 c.c., an increase of 20.8 per cent above the normal level.

#### Total Phosphorus.

-oOo-

Whole Blood: The total phosphorus content of the whole blood was 42.4 mg. per 100 c.c., an increase of 5.7 per cent above the normal average.

Plasma: The total phosphorus content of the plasma was 13.6 mg. per 100 c.c., an increase of 3.6 per cent above the normal.

Red Blood Corpuscles: The total phosphorus content of the red blood corpuscles was 97.1 mg. per 100 c.c.,  
an/

an increase of 2.1 per cent above the normal.

### Haematocrit Finding.

-oOo-

The cellular portion of the whole blood was found to be 34.5 p.c. per 100 c.c., an increase of 4 per cent above the normal average.

### Calcium of the Blood Serum.

-oOo-

Calcium content of the blood serum was found to be 11.1 mg. per 100 c.c., which is 3.4 per cent above the normal average for children.

### Summary.

-oOo-

1. The free phosphorus of the whole blood, plasma, and the corpuscles showed a marked tendency to rise in the amount per 100 c.c.
2. The ester phosphorus was slightly increased in the whole blood, very markedly in the plasma, and slightly diminished in the red blood corpuscles.
3. The lipin phosphorus of the whole blood was within the normal limits, markedly diminished in the plasma, and increased in the red blood corpuscles.
4. Total phosphorus was slightly increased in all of them.
5. Calcium of the plasma was above the normal.
6. Cellular portion was increased in the whole blood.



5. Rickets.

-oOo-

The analysis of the blood for phosphorus compounds was made only in one case of rickets. This patient had all the physical and radiological signs of active rickets. The following changes in the partition of the phosphorus compounds were observed:

Free Phosphorus.

-oOo-

Whole Blood: The free phosphorus of the whole blood was 3.21 mg. per 100 c.c., a decrease of 22.6 per cent below the normal.

Plasma: The free phosphorus was 3.32 mg. per 100 c.c. of the plasma, a decrease of 15.5 per cent below the normal level.

Red Blood Corpuscles: The free phosphorus was 2.9 mg. per 100 c.c. of the red blood corpuscles, a decrease of 37.3 per cent below the normal level.

Ester Phosphorus.

-oOo-

Whole Blood: The ester phosphorus was found to be 20.63 mg. per 100 c.c. of the whole blood, a decrease of 7.9 per cent below the normal average.

Plasma: The ester phosphorus was found to be 0.2 mg. per 100 c.c. of the plasma, a decrease of 47.3 per cent below the normal.

Red/

Red Blood Corpuscles: The ester phosphorus was found to be 64.6 mg. per 100 c.c. of the red blood corpuscles, a decrease of 3.9 per cent below the normal level.

Lipin Phosphorus.

-c0o-

Whole Blood: The lipin phosphorus amounted to 12.07 mg. per 100 c.c. of the whole blood, which is 12 per cent below the normal average.

Plasma: The lipin phosphorus of the plasma was found to be 8.55 mg. per 100 c.c., a decrease of 5.6 per cent below the normal average.

Red Blood Corpuscles: The lipin phosphorus of the red blood corpuscles was 19.6 mg. per 100 c.c., which is 15.7 per cent below the normal.

Total Phosphorus.

-c0o-

Whole Blood: The total phosphorus content was 35.91 mg. per 100 c.c. of the whole blood, and this is 10.4 per cent below the normal average for children.

Plasma: The total phosphorus content was 12.07 mg. per 100 c.c. of the plasma, and this is 8 per cent below the normal average.

Red Blood Corpuscles: The total phosphorus was 87.1 mg per 100 c.c. of the red blood corpuscles, and this is 8.4 per cent below the normal average.

Haematocrit/

Haematocrit Finding.

-cCo-

The cellular portion of the whole blood was found to be 31.7 c.c. per 100 c.c. of the whole blood, and this is 4.3 per cent below the normal average.

Calcium Content of the Blood Serum.

-oCo-

The calcium content of the blood serum was found to be 8.14 mg. per 100 c.c., and this is 24.1 per cent below the normal average.

Summary.

-oCo-

1. The free phosphorus showed a marked tendency to diminish in amount per 100 c.c. of the whole blood, plasma, and the red blood corpuscles. The relative proportion between them was disturbed, the red blood corpuscles suffering the greatest diminution in the free phosphorus per 100 c.c.
2. The ester phosphorus of the whole blood, plasma, and the corpuscles were slightly diminished in amount per 100 c.c.
3. The lipin phosphorus of the whole blood, plasma, and the red blood corpuscles showed a tendency to be diminished in amount per 100 c.c., the red blood corpuscles suffering the greatest fall in the lipin phosphorus.

4. The total phosphorus content was slightly diminished in amount per 100 c.c. of the whole blood, plasma, and the corpuscles.
5. The calcium content showed a tendency to fall appreciably.

6. Functional or Orthostatic Albuminuria.

-oOo-

There was only one case of this nature. There was no history of nephritis, and both clinical signs and symptoms of nephritis were completely absent, but the albumin was persistently present in small amounts during the day. The blood was analysed for the phosphorus compounds in order to see if any changes occur in the partition of the phosphorus compounds. The following changes were noted:

Free Phosphorus.

-oOo-

Whole Blood: The free phosphorus of the whole blood was 4.87 mg. per 100 c.c., and this is 17.3 per cent above the normal average.

Plasma: The free phosphorus of the plasma was 5.57 mg. per 100 c.c., and this is 41.7 per cent above the normal average.

Red Blood Corpuscles: The free phosphorus of the red/



red blood corpuscles was 3.6 mg. per 100 c.c., and this is 22.2 per cent below the normal average.

#### Ester Phosphorus.

-c0o-

Whole Blood: The ester phosphorus was 21.3 mg. per 100 c.c. of the whole blood, which is 4.9 per cent below the normal average.

Plasma: The ester phosphorus was 0.49 mg. per 100 c.c. of the plasma, which is 30 per cent above the normal average.

Red Blood Corpuscles: The ester phosphorus was 57.8 mg. per 100 c.c. of the red blood corpuscles, which is 14 per cent below the normal average.

#### Lipin Phosphorus.

-c0o-

Whole Blood: The lipin phosphorus of the whole blood was 10.22 mg. per 100 c.c., a decrease of 25.6 per cent below the normal average.

Plasma: The lipin phosphorus of the plasma was 9.81 mg. per 100 c.c., an increase of 8.2 per cent above the normal average.

Red Blood Corpuscles: The lipin phosphorus of the red blood corpuscles was 10.9 mg. per 100 c.c., a decrease of 53.1 per cent below the normal average.

#### Total Phosphorus.

-c0o-

Whole/

Whole Blood: The total phosphorus content of the whole blood was found to be 36.12 mg. per 100 c.c., which is 10 per cent below the normal level.

Plasma: The total phosphorus content of the plasma was found to be 15.87 mg. per 100 c.c., which is 20.9 per cent above the normal level.

Red Blood Corpuscles: The total phosphorus of the red blood corpuscles was found to be 71.6 mg. per 100 c.c., which is 24.7 per cent below the normal level.

#### Haematocrit Finding.

-c0o-

The cellular portion of the whole blood was found to be 36.3 c.c. per 100 c.c., which is 9.5 per cent above the normal average.

#### Summary.

-c0o-

1. The free phosphorus was appreciably increased in the amount per 100 c.c., of the whole blood, markedly increased in the plasma, and markedly decreased in the red blood corpuscles. The relationship between them was disturbed.
2. The ester phosphorus of the whole blood was slightly diminished, of the plasma appreciably increased, and of the red blood corpuscles appreciably diminished in the amount per cent.
3. The lipin phosphorus showed a tendency to be appreciably diminished/

diminished in the whole blood, slightly increased in the plasma, and very markedly diminished in the red blood corpuscles per 100 c.c.

4. The total phosphorus was appreciably decreased in the whole blood, appreciably increased in the plasma, and markedly decreased in the red blood corpuscles per 100 c.c.

-----

#### 7. Lymphadenoma.

-oOo-

Among other diseases studied there was a case of lymphadenoma, and the following changes in the partition of the phosphorus compounds of the blood were noted:

#### Free Phosphorus.

-cOo-

Whole Blood: The free phosphorus of the whole blood was 4.06 mg. per 100 c.c., and this is only 2.1 per cent below the normal average.

Plasma: The free phosphorus of the plasma was 4.2 mg. per 100 c.c., and this is 7 per cent above the normal average.

Red Blood Corpuscles: The free phosphorus of the red blood corpuscles was 3.79 mg. per 100 c.c., and this is 18.1 per cent below the normal average.

#### Ester Phosphorus.

Ester Phosphorus.

-c0o-

Whole Blood: The ester phosphorus of the whole blood was 19.83 mg. per 100 c.c., which is 11 per cent below the normal level.

Plasma: The ester phosphorus of the plasma was 10.36 mg. per 100 c.c., which is 5.2 per cent below the normal level.

Red Blood Corpuscles: The ester phosphorus of the red blood corpuscles was 57.1 mg. per 100 c.c., which is 15 per cent below the normal level.

Lipin Phosphorus.

-c0o-

Whole Blood: The lipin phosphorus of the whole blood was 11.74 mg. per 100 c.c., a decrease of 14.5 per cent below the normal level.

Plasma: The lipin phosphorus of the plasma was 6.08 mg. per 100 c.c., a decrease of 32.8 per cent below the normal level.

Red Blood Corpuscles: The lipin phosphorus of the red blood corpuscles was 22.6 mg. per 100 c.c., a decrease of only 2.8 per cent below the normal.

Total Phosphorus.

-c0o-

Whole Blood: The total phosphorus content of the whole/



whole blood was 35.63 mg. per 100 c.c., and this is 11.1 per cent below the normal average.

Plasma: The total phosphorus content of the plasma was 10.69 mg. per 100 c.c., and this is 18.5 per cent below the normal average.

Red Blood Corpuscles: The total phosphorus content of the red blood corpuscles was 83.49 mg. per 100 c.c., and this is 12.2 per cent below the normal average.

#### Haematocrit Finding.

-c0o-

The cellular portion of the whole blood was found to be 34.3 c.c. per 100 c.c., an increase of 3.4 per cent of the normal average.

#### Calcium of the Blood Serum.

-c0o-

The calcium content of the blood serum was found to be 9.8 mg. per 100 c.c., which is 8.9 per cent below the normal average.

#### Summary.

-c0o-

1. The free phosphorus was within normal limits in the whole blood, slightly increased in the plasma, and appreciably decreased in the red blood corpuscles per 100 c.c. The normal relationship between them was disturbed/

disturbed.

2. The ester phosphorus showed a tendency to be slightly diminished in the whole blood, plasma and red blood corpuscles per 100 c.c.
3. The lipin phosphorus suffered an appreciable decrease in the whole blood, a marked decrease in the plasma, and was within normal limits in the red blood corpuscles per 100 c.c.
4. The total phosphorus content showed a tendency to be decreased in amount in the whole blood, the plasma, and the red blood corpuscles per 100 c.c.
4. The calcium content of the blood serum was decreased in amount per 100 c.c.

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#### 8. The Phosphorus partition in a Case of Dwarfism and Effect of Pituitary Extract on the Same.

-000-

This case was a child aet  $9\frac{1}{2}$  years who had stopped growing normally at the age of 5 years. Her actual height was 102.5 cms., whereas the expected height for her age is 128.5 cms. Her actual weight was 16.92 kilograms whereas the expected weight for her age is 27.5 kilos. Her field of vision was within the limits of normality. All the ossification centres of her bones were found practically normal. The X-rays photograph of her skull showed no abnormality. Goetsche's Test was within normal limits.

Though/

Though all the above tests were practically normal the case was considered as a questionable Pituitary Dwarfism. As it was decided to put the patient on Pituitary extract, the opportunity was taken to analyse the blood for the partition of the phosphorus compounds before and after the treatment of 2 months' duration with the pituitary extract.

We propose to discuss first the difference between the partition of the phosphorus compounds of the blood in the case of dwarfism before treatment with pituitary extract and the phosphorus compounds of the blood, of the normal average for children.

#### Free Phosphorus.

-cOo-

The free phosphorus of the whole blood, the plasma, and the red blood corpuscles was found slightly increased in amount per 100 c.c. above the normal average for children. The actual increase expressed in percentage was 5%, 2.5%, and 8% respectively.

#### Ester Phosphorus.

-cOo-

The ester phosphorus was appreciably increased in the amount per 100 c.c. of the whole blood, markedly increased in the amount per 100 c.c. of the plasma, and appreciably increased per 100 c.c. of the red blood corpuscles/

corpuscles . The actual increase expressed in percentage is 10.8% in the whole blood, 76.3% in the plasma, and 9.1% in the red blood corpuscles per 100 c.c. above the normal average.

#### Lipin Phosphorus.

-c0o-

The lipin phosphorus of the whole blood, the plasma, and the red blood corpuscles was markedly diminished in amount per 100 c.c. The actual decrease expressed in percentage is 28%, 14%, and 40.2% respectively below the normal average.

#### Total Phosphorus.

-c0o-

The total phosphorus content of the whole blood, the plasma, and the red blood corpuscles was slightly decreased in amount per 100 c.c. The actual decrease expressed in percentage amounted to 2.8%, 5%, and 2.8% respectively below the normal average for children.

#### Haematocrit Finding.

-c0o-

There was no difference between the cellular portion of the whole blood in the case of dwarfism and that of the normal average for children.

Calcium/



Calcium of the Blood Serum.

-oOo-

The calcium content of the blood plasma was 9.91 per 100 c.c., which amount is 7.6 per cent below the normal average.

Summary.

-cOo-

1. The free phosphorus was very slightly increased per 100 c.c. of the whole blood, the plasma, and the red blood corpuscles.
2. The ester phosphorus showed a tendency to be appreciably increased per cent in the whole blood, plasma and the red blood corpuscles.
3. The lipin phosphorus showed a tendency to be markedly diminished in amount per 100 c.c. of the whole blood, plasma, and the red blood corpuscles.
4. The total phosphorus content was slightly decreased in amount per 100 c.c. of the whole blood, the plasma, and the red blood corpuscles.
5. The calcium content of the blood plasma showed a tendency to be decreased in amount per 100 c.c.

Now we propose to discuss the difference between the partition of the phosphorus of the blood in dwarfism before and after the administration of pituitary extract to the patient. Results are in Table X.

Table X.

The Effect of Pituitary Extract on the Partition of Phosphorus of Blood in a  
Case of Dwarfism.

Time when Blood examined.	Whole Blood						Plasma					Corpuscles				Haema- tocrit RBCs%	Ca Serum mg.%
	F.P.	F.E.P.	E.P.	L.P.	Comb T.P.	Add. T.P.	F.P.	F.E.P.	E.P.	L.P.	T.P.	F.P.	L.P.	E.P.	T.P.		
	mgm. per 100 c.c.						mgm. per 100 c.c.					mgm. per 100 c.c.					
Before Treat- ment.	4.36	29.2	24.84	9.8	39.13	39.0	4.03	4.7	0.67	7.76	12.46	5.0	13.9	73.4	92.3	33.2	9.91
2 Months after Treatment	3.98	23.6	19.62	10.3	34.2	33.9	3.8	4.1	0.3	8.4	12.5	4.5	16.1	79.4	100.0	24.4	10.9
Difference	-8.7%	-19%	-21%	+5.1%	-12.6%	-13%	-5.7%	-12.8%	-55%	+8.2%	0	-10%	+15.8%	+8.1%	+8.3%	-26.5%	+10%

F.P. = Free Phosphorus: F.E.P. = Free plus Ester Phosphorus: L.P. = Lipin Phosphorus:

T.P. = Total Phosphorus.

Free Phosphorus.

-oOo-

Whole Blood: The free phosphorus of the whole blood was 3.98 mg. per 100 c.c. after the <sup>2 months</sup> treatment with pituitary extract, which is 8.7 per cent smaller than that obtained before treatment.

Plasma: The free phosphorus of the plasma was 3.8 mg. per 100 c.c. after the treatment with the pituitary extract, which is 5.7 per cent smaller than that obtained before the treatment.

Red Blood Corpuscles: The free phosphorus of the red blood corpuscles was 4.5 mg. per 100 c.c., which is 10 per cent smaller than that obtained before the treatment. See chart X.

Ester Phosphorus.

-oOo-

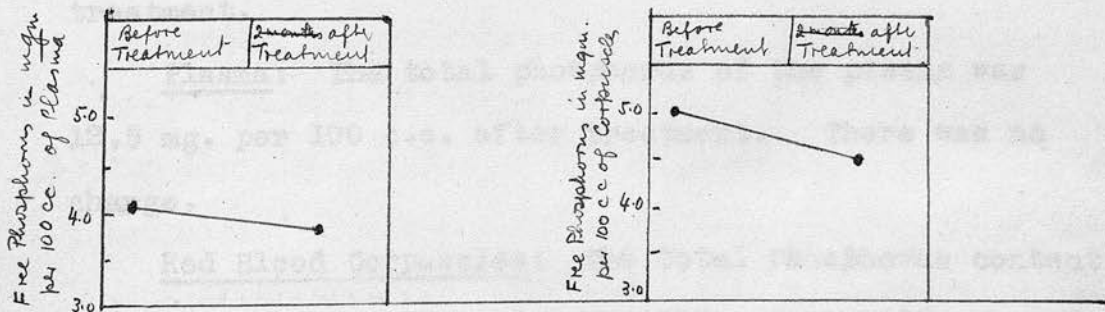
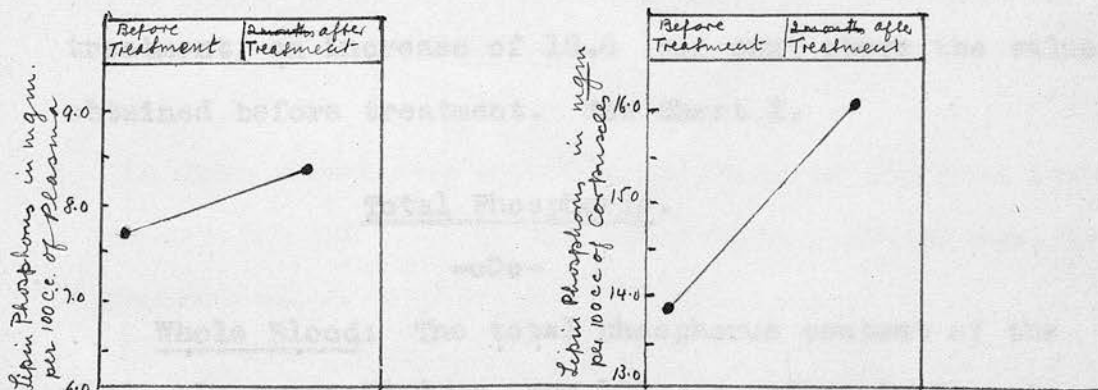
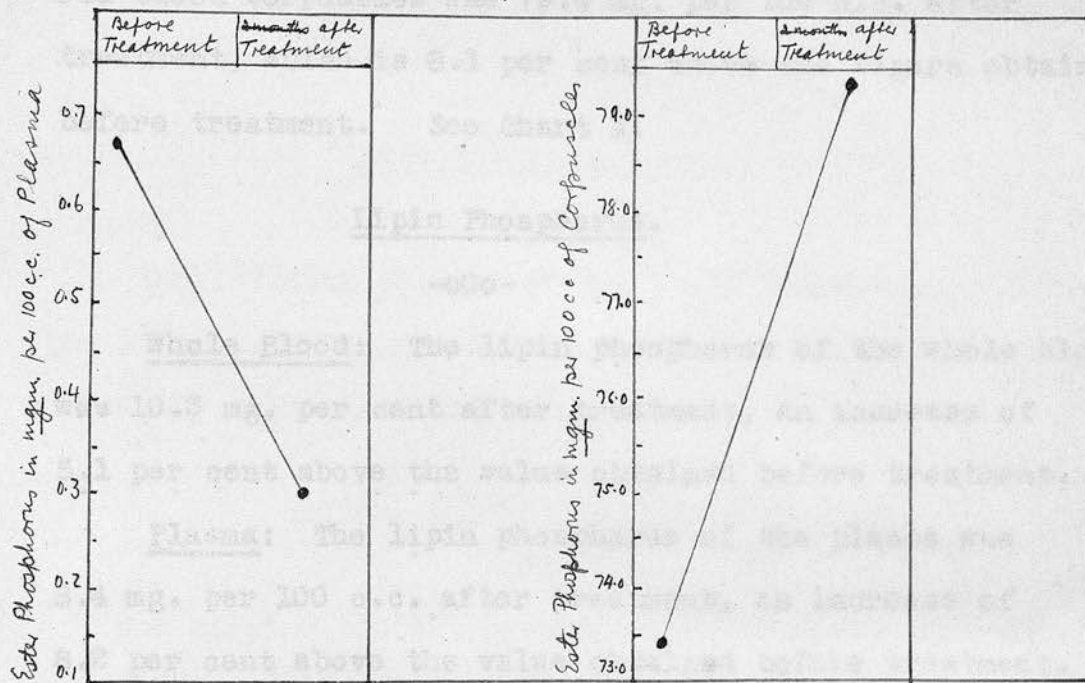
Whole Blood: The ester phosphorus of the whole blood was 19.62 mg. per 100 c.c. after the treatment with the pituitary extract, i.e. 21 per cent below that obtained before treatment.

Plasma: The ester phosphorus of the plasma was 0.3 mg. per 100 c.c. after the treatment, which figure was 55 per cent below that obtained before treatment. See Chart X.

Red Blood Corpuscles: The ester phosphorus of the red/

# Chart X

The Effect of Pituitary Extract on the Partition of Phosphorus Compounds of Blood in a case of Dwarfism.





red blood corpuscles was 79.4 mg. per 100 c.c. after treatment, which is 8.1 per cent above the figure obtained before treatment. See Chart X.

#### Lipin Phosphorus.

-oOo-

Whole Blood: The lipin phosphorus of the whole blood was 10.3 mg. per cent after treatment, an increase of 5.1 per cent above the value obtained before treatment.

Plasma: The lipin phosphorus of the plasma was 8.4 mg. per 100 c.c. after treatment, an increase of 8.2 per cent above the value obtained before treatment.

Red Blood Corpuscles: The lipin phosphorus of the red blood corpuscles was 16.1 mg. per 100 c.c. after treatment, an increase of 15.8 per cent above the value obtained before treatment. See Chart X.

#### Total Phosphorus.

-oOo-

Whole Blood: The total phosphorus content of the whole blood was 33.9 mg. per 100 c.c. after treatment; a decrease of 13 per cent below the value obtained before treatment.

Plasma: The total phosphorus of the plasma was 12.5 mg. per 100 c.c. after treatment. There was no change.

Red Blood Corpuscles: The total phosphorus content of the red blood corpuscles was 100 mg. per 100 c.c. after treatment/

treatment, an increase of 8.3 per cent above the value obtained before treatment.

#### Haematocrit Finding.

-c0o-

The cellular portion of the whole blood was 24.4 c.c. per 100 c.c. after treatment, a decrease of 26.5 per cent below the value obtained before treatment.

#### Calcium Content of the Blood Serum.

-c0o-

The calcium content of the blood serum was 10.9 mg. per 100 c.c. after treatment, an increase of 10 per cent above the value obtained before treatment.

#### Summary.

-c0o-

1. The free phosphorus showed a tendency to decrease in amount per 100 c.c. of the whole blood, the plasma, and the red blood corpuscles after treatment.
2. The ester phosphorus of the whole blood and the plasma showed a tendency to be markedly diminished in amount per cent, whereas the ester phosphorus of the red blood corpuscles appreciably increased in amount per cent after treatment with pituitary extract.
3. The lipin phosphorus of the whole blood, plasma, and the corpuscles showed a tendency to increase in amount per cent after treatment with the pituitary extract.

4. The total phosphorus content was appreciably diminished per 100 c.c. of the whole blood, unaltered per 100 c.c. of the plasma, and increased per 100 c.c. of the red blood corpuscles after treatment.
5. The cellular portion of the whole blood was markedly diminished after treatment.
6. The calcium content of the blood plasma was increased after treatment.

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General Discussion.

-c00-

One of the most significant observations forcing itself into prominence from our results on the partition of the phosphorus compounds of the blood in disease is that all the phosphorus fractions are definitely affected by the disease though the individual changes varied greatly in the different diseases. Of the free phosphorus, ester phosphorus, and the lipin phosphorus fractions of the red blood cells the ester phosphorus fraction showed the greatest amount of stability. In healthy children, we demonstrated that the ester phosphorus as well as the lipin phosphorus of the red blood corpuscles were constant ingredients of the corpuscles, but, in disease, the ester phosphorus fraction appeared to suffer less alteration than the lipin phosphorus fraction, which almost invariably suffered, per unit volume of the corpuscles. Price and Jones (1910)<sup>(84)</sup> demonstrated that in disease the red blood corpuscles were large, the average volume of a cell, according to Haden (1925)<sup>(85)</sup> being 1.42 times greater than the normal average volume. Larger cells would indicate a smaller surface area per unit volume of cells, and a smaller total volume of the surface film with a relatively larger volume of those constituents which do not occupy the surface. Thus this would support the suggestion that the phosphoric esters were not on the surface of the cells, but in the interior/



interior, which would be the opposite of the haemoglobin indicated by the experiments of Bürker (1922)<sup>(86)</sup> and Emmons (1927)<sup>(87)</sup> who believed that the pigment was distributed superficially over the cells. Similarly Garter and Grendel (1925)<sup>(88)</sup> stated that the surface of the red blood corpuscles is covered by a layer of the lipin molecules which were 2 molecules thick, and it would follow from this that the smaller the surface of the red blood corpuscles the fewer the lipin molecules per unit volume. If this were true both of the ester phosphorus fraction and the lipin molecules it would not be idle to suggest that (1) the ester phosphorus fraction, being situated in the interior of the cells, would be less likely affected, for, within limits, the fewer the red blood cells the greater their size, and they could thus accommodate relatively greater amounts of the phosphoric esters. (2) The amount of the lipin phosphorus would depend directly upon the sum total of the surface of the cells, and (3) the lipin phosphorus being lodged on the surface of the cells might further account for its lability, for it would be more likely than not, that under the stress of disease, the superficial layers of the red blood corpuscles would be the first to bear its brunt.

We propose to attempt grouping, and discussing various diseases according to the phosphoric changes of the blood.

Free Phosphorus:

In acute nephritis, tetany, idiopathic convulsions, ununited fracture of tibia, and orthostatic albuminuria the free phosphorus was increased uniformly in the amount per 100 c.c. of the whole blood, the plasma, and the corpuscles, except in the case of orthostatic albuminuria where it was increased both in the whole blood, and the plasma, but showed equally marked decrease in the corpuscles. On the other hand, in Diabetes mellitus, purpura simplex, and rickets the free phosphorus was decreased in the amount by more than 15 per cent below the normal average. See Table XI. In the case of lymphadenoma, dwarfism, and secondary anaemia the free phosphorus fraction was within the limits of normality except in the case of lymphadenoma in which the free phosphorus of the red blood corpuscles showed an appreciably drop. See Chart XI.

Ester Phosphorus:

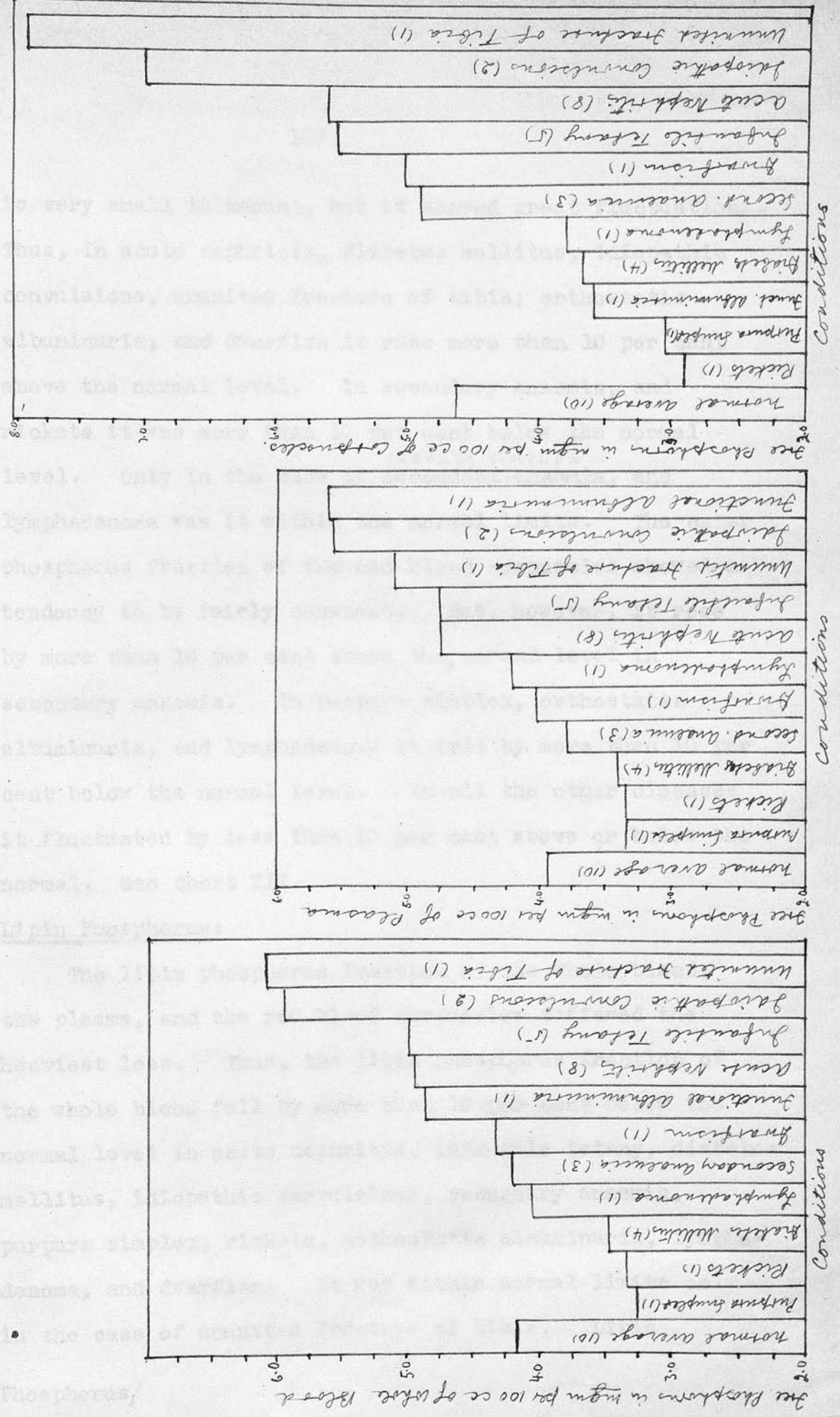
The ester phosphorus of the whole blood, plasma and the red blood corpuscles showed no uniformity in the increase or decrease per cent. Thus, the ester phosphorus of the whole blood was 10 per cent or more below the normal average in the case of idiopathic convulsions, secondary anaemia, purpura simplex, and lymphadenoma. Only in the case of dwarfism did it rise over 10 per cent above the normal level. In all the other diseases reported here it was less than 10 per cent above or below the normal average. The ester phosphorus fraction of the plasma is/

Table XI.

Results expressed in Percentage.

Diseases.	Whole Blood				Plasma				Corpuscles				Haema- tocrit RBCs %	Ca. Ser- um.
	F.P.	L.P.	E.P.	T.P.	F.P.	L.P.	E.P.	T.P.	F.P.	L.P.	E.P.	T.P.		
1. Normal Average (10)	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
2. Average for Acute Nephritis (8)	119.0	90.0	93.3	95.2	119.0	97.7	113.1	106.4	120.9	86.7	104.5	101.0	90.5	89.1
3. Average for Inf. Tetany (5)	120.	72.5	95.6	90.4	120.8	71.6	79.0	87.5	118.7	75.0	99.0	94.1	96.0	53.4
4. Average Diabetes Mellitus (4)	83.7	74.3	96.8	88.2	85.3	101.5	126.3	100.0	79.5	51.5	91.3	81.0	105.5	100.0
5. Average for Idiop. Convulsions (2)	142.0	77.4	81.6	86.9	141.0	69.2	140.0	94.1	151.0	100.0	100.0	102.0	80.3	-
6. Average for Sec. Anaemia (3)	100.0	76.5	88.0	86.5	100.0	94.5	73.7	96.8	100.0	71.0	117.0	104.9	75.8	95.7
7. Purpura Simplex (1)	78.1	66.0	77.5	74.0	84.5	79.5	100.0	81.0	66.4	59.	89.7	81.0	85.2	103.0
8. Ununited Fracture of Tibia (1)	147.0	96.4	103.1	105.7	130.5	59.6	808.0	103.6	170.6	120.8	91.0	102.1	104.0	103.4
9. Rickets (1)	77.4	88.0	92.1	89.6	84.5	94.4	52.7	92.0	62.7	84.3	96.1	91.6	95.7	75.9
10. Functional Albumin-uria (1)	117.3	74.4	95.1	90.0	141.7	108.2	130.0	120.9	77.8	46.9	86.0	75.3	109.5	-
11. Lymphadenoma (1)	97.9	85.5	89.0	88.9	107.0	67.2	94.8	81.5	81.9	97.2	85.0	87.8	103.4	91.1
12. Dwarfism (1)	105.0	72.0	110.8	97.2	102.5	86.0	176.3	95.0	108.0	59.8	109.1	97.2	100.0	92.4

Chart XI — Showing Free Phosphorus of the Whole Blood, Plasma, and Cerebrospinal in different diseases.



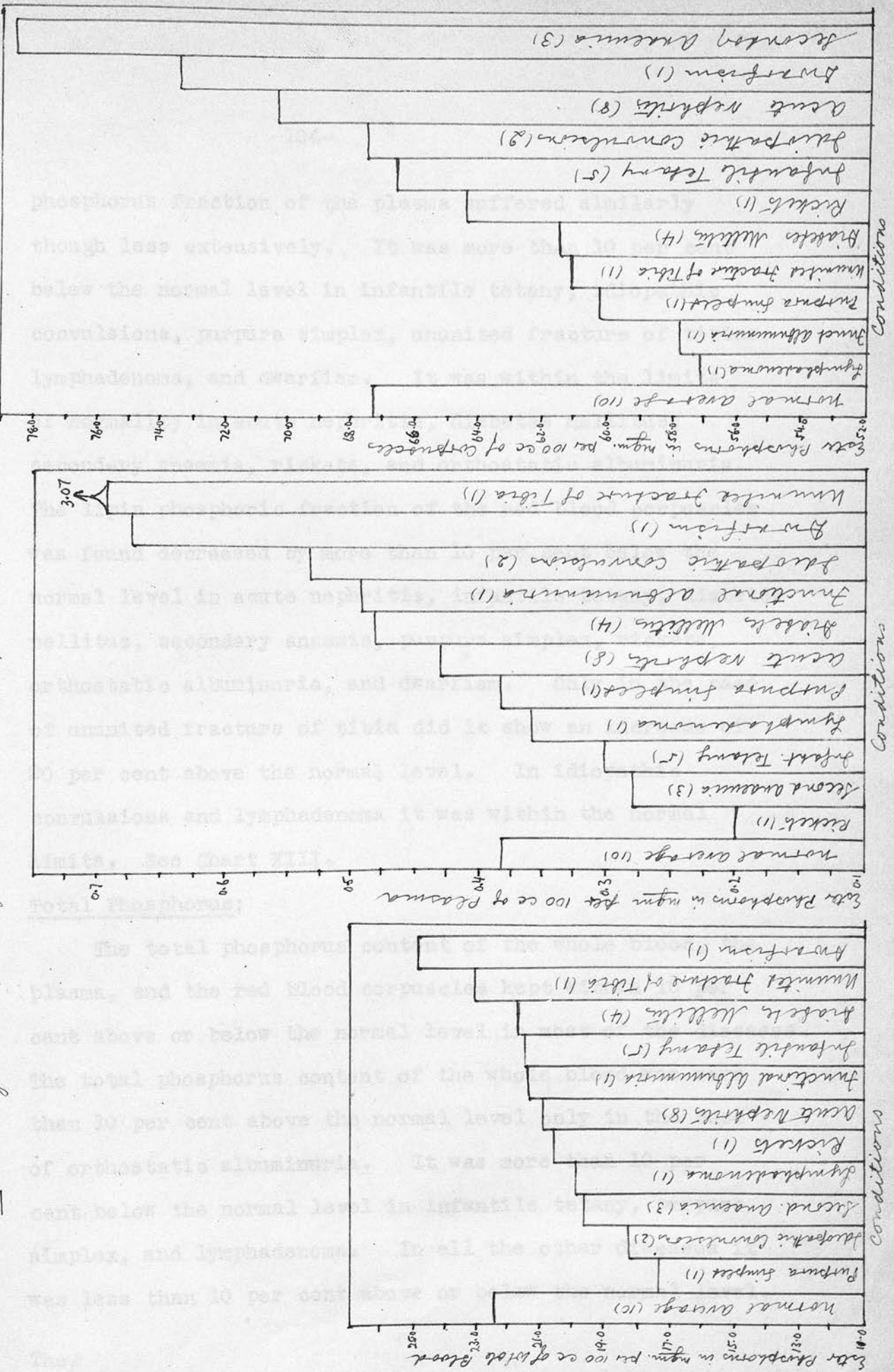


is very small in amount, but it showed great fluctuations. Thus, in acute nephritis, diabetes mellitus, idiopathic convulsions, ununited fracture of tibia, orthostatic albuminuria, and dwarfism it rose more than 10 per cent above the normal level. In secondary anaemia, and rickets it was more than 10 per cent below the normal level. Only in the case of <sup>PURPURA SIMPLEX</sup> ~~secondary anaemia~~, and lymphadenoma was it within the normal limits. The ester phosphorus fraction of the red blood corpuscles showed a tendency to be fairly constant. But, however, it rose by more than 10 per cent above the normal level in secondary anaemia. In purpura simplex, orthostatic albuminuria, and lymphadenoma it fell by more than 10 per cent below the normal level. In all the other diseases it fluctuated by less than 10 per cent above or below the normal. See Chart XII.

#### Lipin Phosphorus:

The lipin phosphorus fraction of the whole blood, the plasma, and the red blood corpuscles suffered the heaviest loss. Thus, the lipin phosphorus fraction of the whole blood fell by more than 10 per cent below the normal level in acute nephritis, infantile tetany, diabetes mellitus, idiopathic convulsions, secondary anaemia, purpura simplex, rickets, orthostatic albuminuria, lymphadenoma, and dwarfism. It was within normal limits only in the case of ununited fracture of tibia. Lipin

Chart XII - Showing Ester Phosphorus of the whole Blood, Plasma, and Corpuscles in different Diseases.



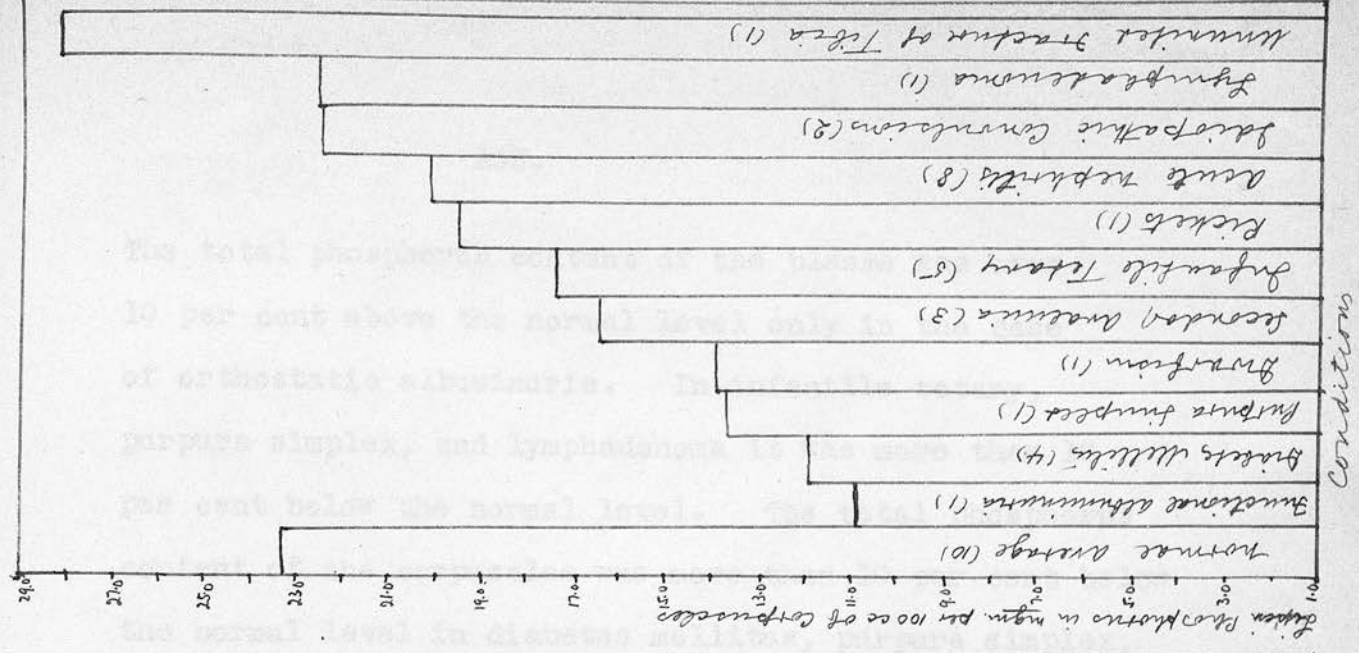
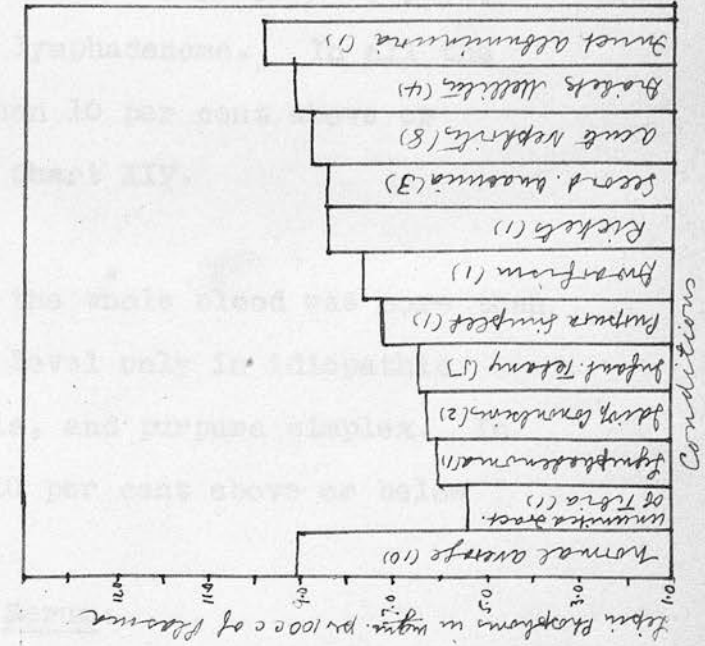
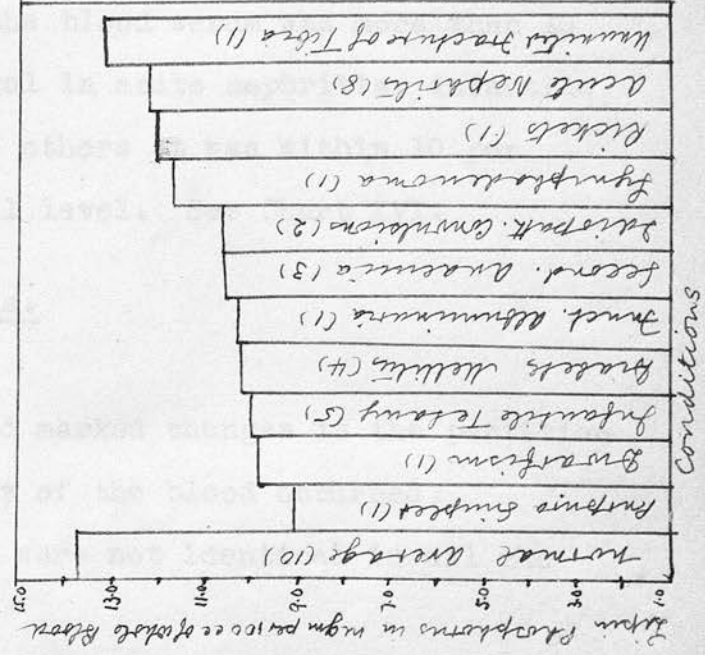
phosphorus fraction of the plasma suffered similarly though less extensively. It was more than 10 per cent below the normal level in infantile tetany, idiopathic convulsions, purpura simplex, ununited fracture of tibiae, lymphadenoma, and dwarfism. It was within the limits of normality in acute nephritis, diabetes mellitus, secondary anaemia, rickets, and orthostatic albuminuria. The lipin phosphoric fraction of the red blood corpuscles was found decreased by more than 10 per cent below the normal level in acute nephritis, infantile tetany, diabetes mellitus, secondary anaemia, purpura simplex, rickets, orthostatic albuminuria, and dwarfism. Only in the case of ununited fracture of tibia did it show an increase of 20 per cent above the normal level. In idiopathic convulsions and lymphadenoma it was within the normal limits. See Chart XIII.

Total Phosphorus:

The total phosphorus content of the whole blood, the plasma, and the red blood corpuscles kept within 10 per cent above or below the normal level in most of the diseases. The total phosphorus content of the whole blood was more than 10 per cent above the normal level only in the case of orthostatic albuminuria. It was more than 10 per cent below the normal level in infantile tetany, purpura simplex, and lymphadenoma. In all the other diseases it was less than 10 per cent above or below the normal level.

The/

Chart XIII - Showing Lipin Phosphorus of the whole Blood, Plasma, and corpuscles in different Diseases.





The total phosphorus content of the plasma was over 10 per cent above the normal level only in the case of orthostatic albuminuria. In infantile tetany, purpura simplex, and lymphadenoma it was more than 10 per cent below the normal level. The total phosphorus content of the corpuscles was more than 10 per cent below the normal level in diabetes mellitus, purpura simplex, orthostatic albuminuria, and lymphadenoma. In all the other diseases it was less than 10 per cent above or below the normal level. See Chart XIV.

#### Haematocrit:

The cellular portion of the whole blood was more than 10 per cent below the normal level only in idiopathic convulsions, secondary anaemia, and purpura simplex. In the others it was less than 10 per cent above or below the normal. See Chart XV.

#### Calcium Content of the Blood Serum:

The calcium content of the blood serum was more than 10 per cent below the normal level in acute nephritis, infantile tetany, and rickets. In the others it was within 10 per cent above or below the normal level. See Chart XVI.

#### Conclusions.

-oOo-

1. In all the diseases studied marked changes in the partition of the phosphorus compounds of the blood occurred.
2. The changes which occurred were not identical in all the diseases/

Chart XIV - Showing Total Phosphorus Content of the Whole Blood, Plasma, and Corpuscles in different Diseases.

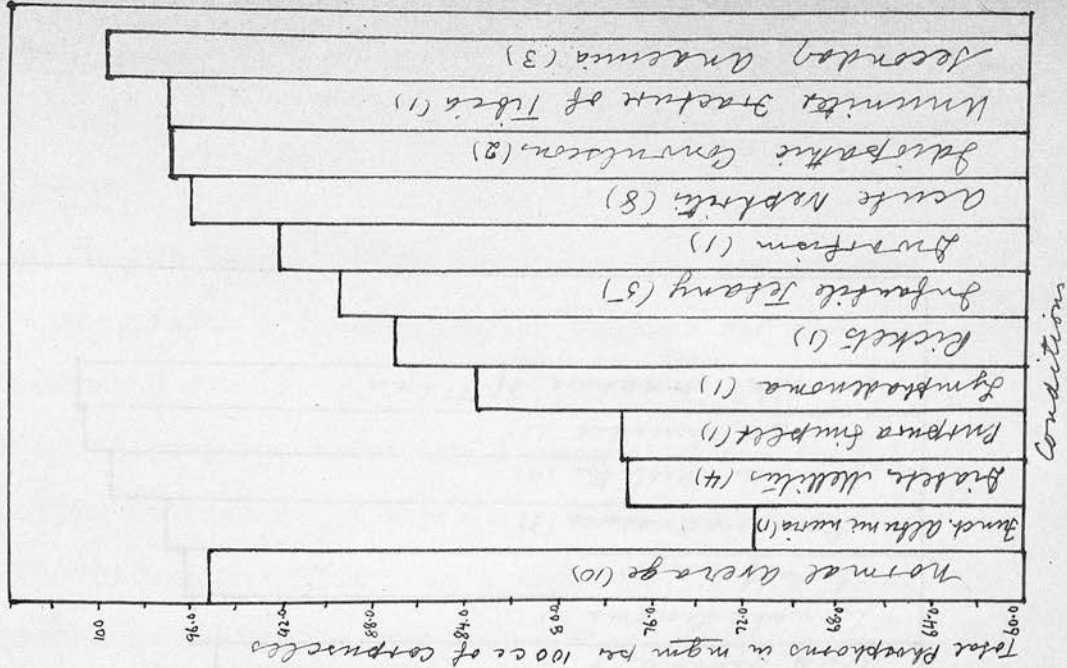
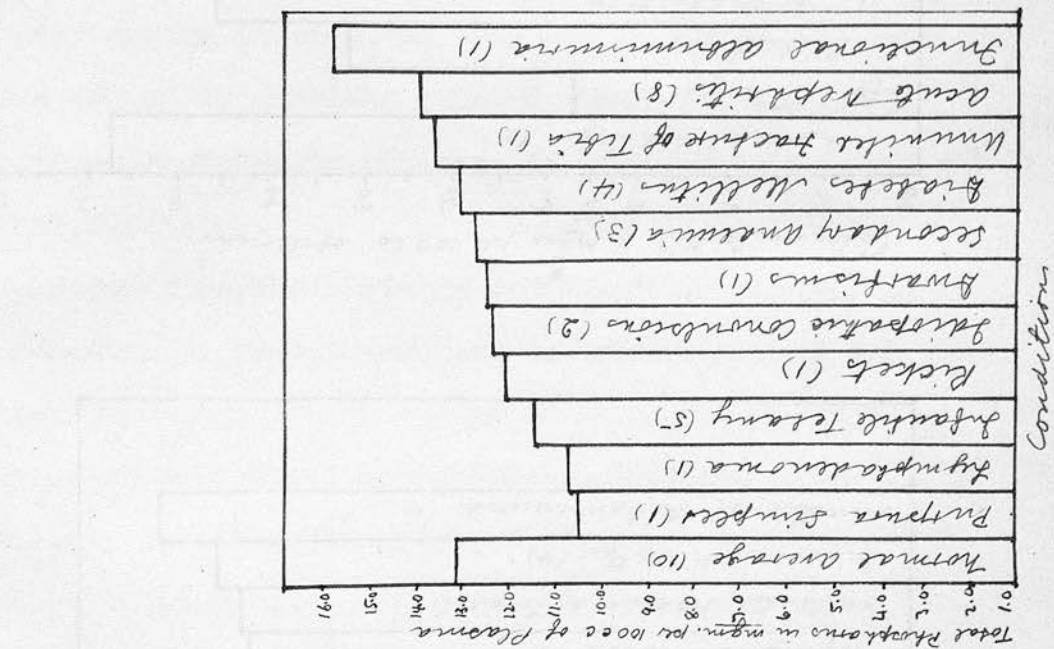
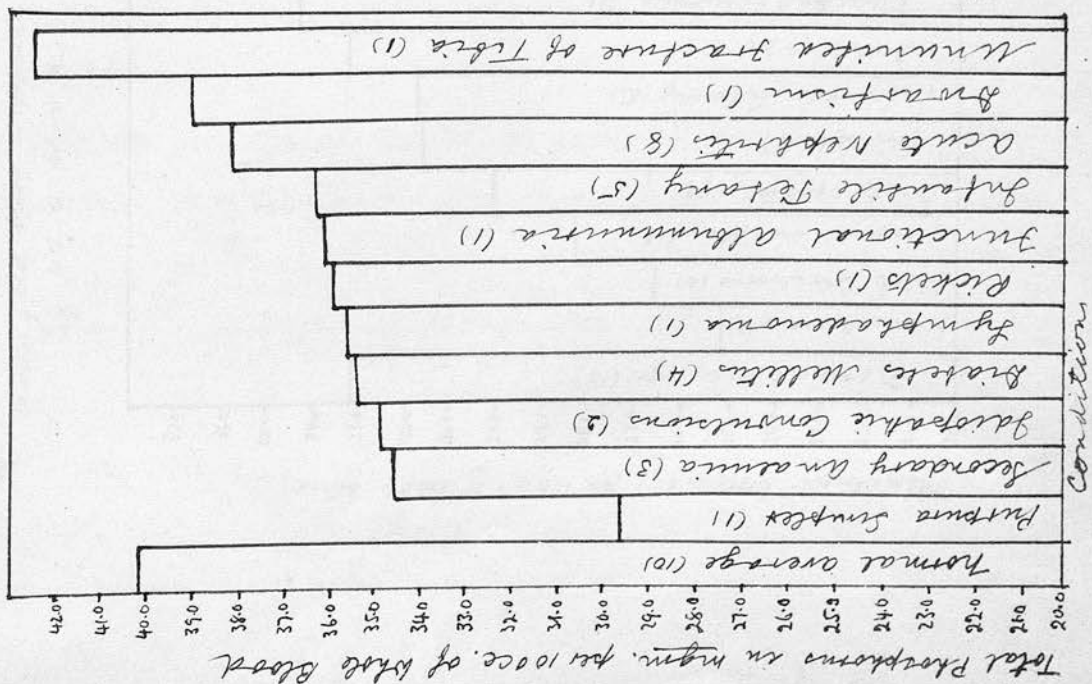


Chart XV -

Showing red blood corpuscles in cc. per 100 cc of white blood

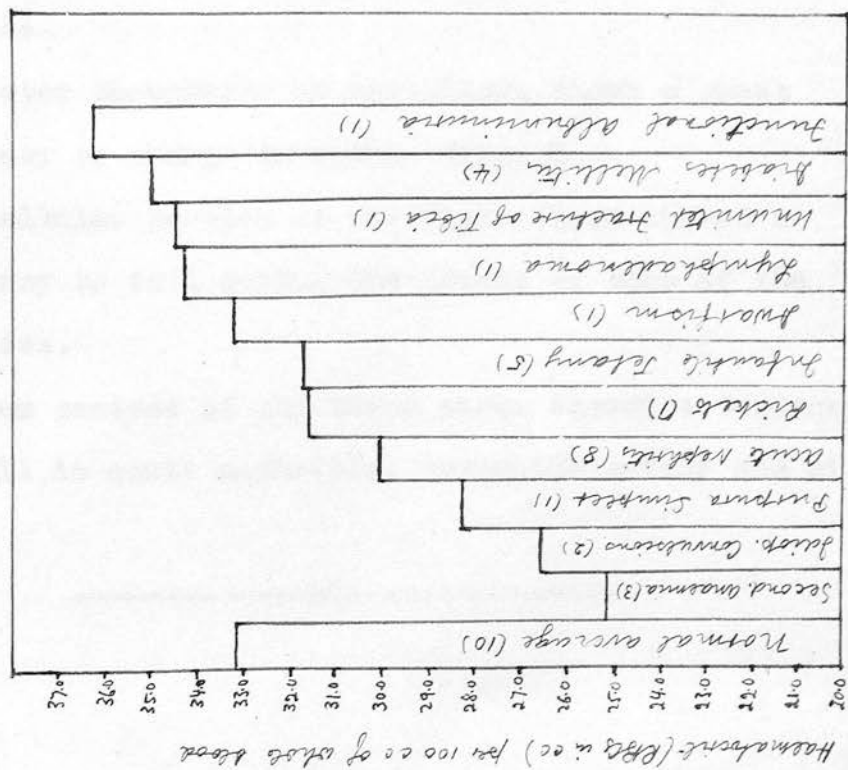
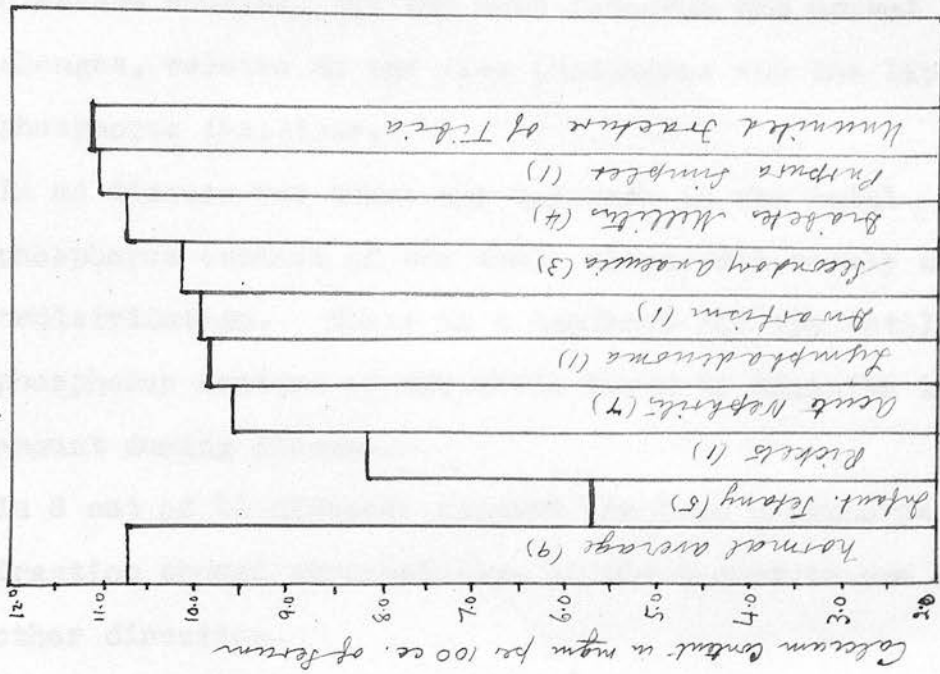


Chart XVI - Showing Calcium content of serum.



diseases studied, but the most frequent and marked changes, related to the free phosphorus and the lipin phosphorus fractions.

3. In no disease was there any increase in the total phosphorus content of the whole blood, but merely a redistribution. There is a tendency for the total phosphorus content of the whole blood to diminish in amount during disease.
4. In 8 out of 11 diseases studied the free phosphorus fraction showed abnormalities in the amount in one or other direction.
5. The ester phosphorus of the red blood corpuscles shows a tendency to remain constant in amount during the disease.
6. The ester phosphorus of the plasma shows a great tendency to change in either direction.
7. The cellular portion of the whole blood showed a tendency to fall during the course of some of the diseases.
8. Calcium content of the blood serum showed a tendency to fall in acute nephritis, infantile tetany and rickets.

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P A R T IV.The Effect of Deep X-rays Therapy on the Partition of  
the Phosphorus Compounds of the Blood in  
Different Diseases.

-oOo-

In the course of the present study of the distribution of the phosphorus of the blood in health and disease, it happened that the blood for phosphorus compounds in the case of lymphadenoma was examined on two different occasions. While comparing these results we were impressed with the marked changes that took place in the lipin phosphorus of the plasma, and in the red blood corpuscles. There seemed to have occurred a shift of the lipin phosphorus of the red blood corpuscles into the plasma. Knowing that the patient had received a therapeutic dose of X-rays soon after the first analysis of the blood the question naturally arose as to whether this redistribution of the phosphorus compounds might be directly due to the effect of X-rays. Within a couple of months the patient was due to have another treatment with X-rays, and that opportunity was taken to confirm our suspicion. The experiment was repeated, and practically the same changes were observed to take place in the phosphorus compounds - especially in the lipin phosphorus - of the blood. In order to test the verity of these findings further, we decided to extend this study to some other cases treated with X-rays irradiation. Soon afterwards we had an opportunity/

opportunity to carry out the same experiment on the blood of a case suffering from haemangioma of the thigh. The results were again very similar to those previously obtained.

It was felt that these changes might be more marked in a case of intense X-rays therapy e.g. deep X-rays, and, through the courtesy of Dr. S.D.Scott Park of the Western Infirmary, Glasgow, we were enabled to repeat our examinations of the blood in a case of carcinoma of the mamma and one suffering from a cerebral cyst. It seemed all the more important to extend our investigations as a search of the literature only revealed one reference to this aspect of the subject.

The procedure adopted for the experiments was exactly the same in all of them. First, a specimen of blood was obtained from a vein in the arm of each patient after a whole night's starvation, and all the estimations of the phosphorus compounds were carried out immediately. At varying intervals after the patients had been exposed to deep X-rays irradiation another specimen of blood was obtained under the same condition as on the first occasion, and analysis proceeded with at once.

In view of the fact that these 4 patients were suffering from different pathological condition, and in case that the disease itself might have influenced the phosphorus partition, and caused a different change, it is proposed to/

to take, and discuss the findings of each one in turn. The results of all the experiments are in Table XII.

Lymphadenoma.

-oOo-

The relative changes in the partition of the phosphorus compounds of the blood in this case of lymphadenoma in comparison with the standard of normality were discussed fully on the pages 89, 90, 91, and 92.

In the two independent experiments on the action of X-rays therapy on the partition of the phosphorus compounds in the blood the following changes were observed: (it is well to bear in mind that for the ensuing comparison between different fractions of the phosphorus compounds the results from the first specimen of the blood are used as the standard and not the standard of normality).

Experiment 1.

Free Phosphorus.

-oOo-

The free phosphorus was found to be very slightly diminished in amount per 100 c.c. of the whole blood, the plasma, and the red blood corpuscles after the application of X-rays irradiation. The actual decrease in the amount was 1.9%, 2.3%, and 1.5% respectively.

Ester/

TABLE XII - The Effect of X-ray Therapy on the partition  
of Phosphorus compounds in the  
Blood.

NAME & AGE.	TIME WHEN BLOOD EXA- MINED.	W H O L E B L O O D.						P L A S M A.					C O R P U S C L E S.				Haema- tocrit.
		F.P.	F.E.P.	E.P.	L.P.	Comb. T.P.	Add. T.P.	F.P.	F.E.P.	E.P.	L.P.	T.P.	F.P.	L.P.	E.P.	T.P.	R.B.Cs %
			mgm. per 100 cc.						mgm per 100 cc.					Mgm. per 100 cc.			
1. H.M. 8yrs	Before X-rays.	4.06	23.89	19.83	17.74	36.13	35.63	4.2	4.56	0.36	6.08	10.69	3.79	22.6	57.1	83.49	34.3
	5 days after X-rays.	3.98	25.47	21.49	10.75	36.63	36.22	4.11	4.52	0.41	7.15	11.76	3.73	17.5	60.9	82.13	34.8
2. M.H. 8 "	Before X-rays.	3.84	23.0	19.16	12.47	36.2	35.47	3.9	4.25	0.35	8.95	13.2	3.7	21.0	64.9	89.6	29.1
	24 hrs after X-rays	3.95	25.0	21.05	13.3	38.1	38.3	3.8	4.3	0.5	10.7	15.0	4.2	18.0	58.3	80.5	35.5
	5 days after X-rays.	4.09	24.8	20.71	12.8	37.8	37.6	3.9	4.35	0.45	10.85	15.2	4.5	16.8	62.4	83.7	32.7
3. C.M. 7 "	Before X-rays.	4.08	27.1	23.02	12.8	40.6	39.9	4.15	4.48	0.33	8.72	13.2	3.9	20.1	63.8	87.8	35.7
	33 hrs. after X-rays.	3.54	25.0	21.46	11.1	35.6	36.1	3.85	4.3	0.45	9.4	13.7	2.9	14.54	62.7	80.14	33.7
4. E.McA 60"	Before X-rays	3.01	30.8	27.79	9.0	40.6	39.8	2.9	3.1	0.2	5.0	8.06	3.4	15.2	70.5	89.1	39.4
	46 hrs. after X-rays	2.99	30.4	27.41	9.3	40.1	39.7	2.4	2.8	0.4	7.2	10.0	3.9	12.5	68.6	85.0	39.6
5. J.B. 33"	Before X-rays.	2.63	19.6	16.97	12.2	30.9	31.8	2.3	2.6	0.3	7.2	9.8	3.3	22.2	50.3	75.8	33.3
	3 days after X-rays	2.85	19.2	16.35	11.8	31.4	31.0	2.7	3.3	0.6	8.7	12.0	3.1	17.5	45.3	65.9	35.2

F.P. - Free phosphorus; F.E.P. - Free plus este phosphorus; L.P. - Lipin Phosphorus; T.P. - Total Phosphorus content



Ester Phosphorus.

-oOo-

The ester phosphorus was found to be slightly increased in amount per 100 c.c. of the whole blood, the plasma, and the red blood corpuscles after X-rays irradiation. The actual increase expressed in percentage was 8.3%, 14%, and 6.6% respectively.

Lipin Phosphorus.

-oOo-

Whole Blood: The lipin phosphorus of the whole blood was 10.75 mg. per 100 c.c. after the irradiation, and this is 8.4 per cent below the control value.

Plasma: The lipin phosphorus of the plasma was found to be 7.15 mg. per 100 c.c. after the irradiation, and this is 17.8 per cent above the control.

Red Blood Corpuscles: The lipin phosphorus of the red blood corpuscles was found to be 17.5 mg. per 100 c.c., and this is 22.6 per cent below the control.

Total Phosphorus.

-oOo-

The total phosphorus content was slightly increased in amount per 100 c.c. of the whole blood, appreciably increased in the plasma, and very slightly decreased in the red blood corpuscles per cent. The actual increase expressed in percentage was 1.6% for the whole blood, and 8.6%.

8.6% for the plasma. The actual decrease in the red blood corpuscles was 1.6%.

Haematocrit Finding.

-oOo-

There was no appreciable change in the cellular portion of the whole blood per cent as the result of X-rays irradiation.

Summary.

-oOo-

1. The free phosphorus was very slightly decreased in the amount per cent of the whole blood, the plasma, and the red blood corpuscles.
2. The ester phosphorus was appreciably increased in amount per cent of the whole blood, and the plasma, and slightly increased per cent in the red blood corpuscles.
3. The lipin phosphorus was appreciably decreased in the whole blood, and markedly so in the red blood corpuscles per cent, whereas it increased markedly in the plasma per cent.
4. The total phosphorus content was slightly increased in the whole blood, and the plasma, whereas slightly decreased in the red blood corpuscles per cent.

-----

Experiment/

Experiment 2.

-oOo-

In this experiment the blood was analysed twice after the X-rays irradiation, but as the results of both of them were similar, only the results of the analysis of blood 5 days after irradiation will be discussed here.

Free Phosphorus.

-oOo-

Whole Blood: The free phosphorus of the whole blood was 4.09 mg. per 100 c.c. 5 days after the administration of X-rays irradiation, which is 6.5 per cent above the control value.

Plasma: The free phosphorus of the plasma was 3.9 mg. per 100 c.c., which is exactly the same as that of the control.

Red Blood Corpuscles: The free phosphorus of the red blood corpuscles was 4.5 mg. per 100 c.c., which is 21.6 per cent above the control value.

Ester Phosphorus.

-cOo-

Whole Blood: The ester phosphorus of the whole blood was 20.71 mg. per 100 c.c., which is 8 per cent above the control.

Plasma: The ester phosphorus of the plasma was 0.45 mg. per 100 c.c., which is 28.5 per cent above the control value.

Red Blood Corpuscles: The ester phosphorus of the red blood/

blood corpuscles was 62.4 mg. per 100 c.c., which is 3.8 per cent below the control value.

#### Lipin Phosphorus.

-c0o-

Whole Blood: The lipin phosphorus of the whole blood was 12.8 mg. per 100 c.c., i.e. 2.6 per cent above the control value.

Plasma: The lipin phosphorus of the plasma was 10.85 mg. per 100 c.c., or 21.2 per cent above the control value.

Red Blood Corpuscles: The lipin phosphorus of the red blood corpuscles was 16.8 mg. per 100 c.c., i.e. 20 per cent below the control value.

#### Total Phosphorus.

-c0o-

Whole Blood: The total phosphorus content of the whole blood was 37.6 mg. per 100 c.c., which is 6 per cent above the control value.

Plasma: The total phosphorus of the plasma was 15.2 mg. per 100 c.c., which is 15.1 per cent above the control value.

Red Blood Corpuscles: The total phosphorus content of the red blood corpuscles was 83.7 mg. per 100 c.c., which is 6.5 per cent below the control value.

#### Haematocrit Finding.

-c0o-

The cellular portion of the whole blood was 32.7 c.c. per/



per 100 c.c., which is 12.3 per cent above the control value.

#### Summary.

-c0o-

1. The free phosphorus showed a tendency to increase in amount per 100 c.c. of the whole blood, and the red blood corpuscles. In the plasma it remained constant.
2. The ester phosphorus showed a tendency to rise in the whole blood, and the plasma per 100 c.c., and in the corpuscles it slightly fell in amount per 100 c.c. after the application of X-ray irradiation.
3. The lipin phosphorus showed a tendency slightly to rise in the whole blood, appreciably in the plasma, and fell markedly in the red blood corpuscles per 100 c.c. after the irradiation.
4. The total phosphorus content showed a tendency to rise in the whole blood, and the plasma, and to fall in the red blood corpuscles per 100 c.c.
5. The cellular portion of the whole blood showed a tendency to rise after the treatment.

-----

#### Experiment 3.

-c0o-

This patient was suffering from haemangioma of the thigh. The blood analysis was done before the application of X-rays therapy, and it was done again 33 hours after X-rays irradiation/

irradiation. From the two observations the following changes appeared in the partition of the phosphorus compounds in the blood after the irradiation.

#### Free Phosphorus.

-c0o-

Whole Blood\* The free phosphorus of the whole blood was 3.54 mg. per 100 c.c. after treatment and this is 13.2 per cent below the control value.

Plasma: The free phosphorus of the plasma was 3.85 mg. per 100 c.c. after treatment, and this is 7.2 per cent below the control value.

Red Blood Corpuscles: The free phosphorus of the red blood corpuscles after the treatment was 2.9 mg. per 100 c.c., and this is 25.6 per cent below the control value.

#### Ester Phosphorus.

-c0o-

Whole Blood: The ester phosphorus of the whole blood after the treatment was 21.46 mg. per 100 c.c., and this is a decrease of 6.7 per cent.

Plasma: The ester phosphorus of the plasma after treatment was 0.45 mg. per 100 c.c., and this is 36.3 per cent above the control value.

Red Blood Corpuscles: The ester phosphorus of the red blood corpuscles was 62.7 mg. per 100 c.c., and this is 1.7 per cent below the control value.

Lipin Phosphorus.

-c0o-

Whole Blood: The lipin phosphorus of the whole blood after treatment was 11.1 mg. per 100 c.c., which is 13.2 per cent below the control value.

Plasma: The lipin phosphorus of the plasma after treatment was 9.4 mg. per 100 c.c., and this is 7.8 per cent above the control value.

Red Blood Corpuscles: The lipin phosphorus of the red blood corpuscles after treatment was 14.54 mg. per 100 c.c., and this is 27.7 per cent below the control value.

Total Phosphorus.

-c0o-

Whole Blood: The total phosphorus content of the whole blood after treatment was 36.1 mg. per 100 c.c., and this is 9.5 per cent below the control.

Plasma: The total phosphorus content of the plasma after treatment was 13.7 mg. per 100 c.c., and this is 3.7 per cent above the control.

Red Blood Corpuscles: The total phosphorus content of the red blood corpuscles after treatment was 80.14 mg. per 100 c.c., and this is 8.7 per cent below the control.

Haematocrit Finding.

-c0o-

The cellular portion of the whole blood after treatment/

treatment was 33.7 c.c. per 100 c.c., and this is 5.3 per cent below the control.

Summary.

-c0o-

1. The free phosphorus showed a tendency to diminish in amount per 100 c.c., of the whole blood, the plasma, and the red blood corpuscles after treatment with X-rays irradiation.
2. The ester phosphorus showed a tendency to diminish in amount in the whole blood, and the red blood corpuscles, and to increase in the plasma per 100 c.c., after treatment.
3. The lipin phosphorus showed a tendency to fall in amount in the whole blood, and the red blood corpuscles, and to rise in amount in the plasma per 100 c.c., after treatment.
4. The total phosphorus content showed a tendency to diminish in the whole blood, and the red blood corpuscles, and to rise in amount in the plasma per 100 c.c. after treatment.
5. The cellular portion of the whole blood showed a tendency to diminish in amount per cent after treatment.

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Experiment 4.

-c0o-

This experiment was carried out on an adult patient,



aet 60 years, suffering from carcinoma of the breast. The blood was analysed, then deep X-rays therapy was applied, and 46 hours later another analysis of the blood was done.

The phosphorus compounds of the blood in case of carcinoma differed from the average for normal adults in the following directions:

(1) The free phosphorus of the plasma of the whole blood, and of the red blood corpuscles was within the limits of normality.

(2) The ester phosphorus of the red blood corpuscles was 33 per cent above the average for normal adults.

(3) The lipin phosphorus of the plasma was 30 per cent, and that of the red blood corpuscles 15.5 per cent below the average for normal adults.

(4) The cellular portion of the whole blood was 8.3 per cent below the normal average for adults.

The following changes in the partition of the phosphorus compounds of the blood in the case of carcinoma were noted after deep X-rays therapy.

#### Free Phosphorus.

-c0o-

Whole Blood: The free phosphorus of the whole blood after treatment was 2.99 mg. per 100 c.c., an amount 0.6 per cent below the control value.

Plasma: The free phosphorus of the plasma after treatment was 2.4 mg. per 100 c.c., i.e. 17 per cent below the/

the control.

Red Blood Corpuscles: The free phosphorus of the red blood corpuscles after treatment was 3.9 mg. per 100 c.c., which is 14.7 per cent above the control value.

Ester Phosphorus.

-c0o-

Whole Blood: The ester phosphorus of the whole blood after treatment was 27.41 per 100 c.c., which is 1.3 per cent below the control value.

Plasma: The ester phosphorus of the plasma after treatment was 0.4 mg. per 100 c.c., representing 100 per cent above the control value.

Red Blood Corpuscles: The ester phosphorus of the red blood corpuscles after treatment was 68.6 mg. per 100 c.c., i.e. 2.8 per cent below the control value.

Lipin Phosphorus.

-c0o-

Whole Blood: The lipin phosphorus of the whole blood after treatment was 9.3 mg. per 100 c.c., or 3.3 per cent above the control.

Plasma: The lipin phosphorus of the plasma after treatment was 7.2 mg. per 100 c.c., or 44 per cent above the control value.

Red Blood Corpuscles: The lipin phosphorus of the red blood corpuscles after treatment was 12.5 mg. per 100 c.c., or 17.7 per cent below the control value.

Total/

Total Phosphorus.

-oOo-

Whole Blood: The total phosphorus content of the whole blood, after treatment, was 39.7 mg. per 100 c.c., i.e. there was no change.

Plasma: The total phosphorus content of the plasma, after treatment, was 10.0 mg. per 100 c.c., i.e. an increase of 24 per cent.

Red Blood Corpuscles: The total phosphorus of the red blood corpuscles, after treatment, was diminished in amount by 4.5 per cent.

Haematocrit Finding.

-oOo-

There was no change in the cellular portion of the whole blood after treatment.

Summary.

-oOo-

1. The free phosphorus remained the same in the whole blood, decreased in the plasma, and increased in the red blood corpuscles after deep X-rays irradiation.
2. The ester phosphorus slightly diminished in the whole blood, was doubled in the plasma, and slightly diminished in amount per 100 c.c. of the red blood corpuscles after treatment.
3. Lipin phosphorus slightly increased in the whole blood, markedly increased in the plasma, and markedly decreased at/

in the red blood corpuscles per 100 c.c. after treatment.

4. The total phosphorus content remained stationary in the whole blood, showed a tendency to increase in the plasma, and was slightly diminished in the red blood corpuscles per 100 c.c. after treatment.

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Experiment 5.

-c0o-

The patient was an adult, aet 33 years, suffering from a cerebral cyst. The blood was analysed, as a control, just before deep X-raystherapy was applied, and again 3 days after the treatment.

The partition of the phosphorus compounds of the control sample of blood differed from the normal average for the adults in the following manner:

- (1) The free phosphorus of the control blood was within the limits of normality.
- (2) The ester phosphorus of the plasma was within the normal limits, and that of the red blood corpuscles was found to be 5 per cent below the normal average for adults.
- (3) The lipin phosphorus of the plasma was within normal limits, and that of the corpuscles was 23.3 per cent above the normal average for adults.
- (4) The cellular portion of the whole blood was 22.5 per cent below the normal average for adults.



The following changes in the partition of the phosphorus compounds of the blood in the case of cerebral cyst occurred as the result of deep X-ray therapy, and in comparison with the partition of the phosphorus compounds of the control blood in the same case before treatment was applied.

#### Free Phosphorus.

-c0o-

Whole Blood: The free phosphorus of the whole blood, after treatment was 2.85 mg. per 100 c.c., and this is 8.3 per cent above the control value.

Plasma: The free phosphorus of the plasma, after treatment, was 2.7 mg. per 100 c.c., and this is 17.3 per cent above the control value.

Red Blood Corpuscles: The free phosphorus of the red blood corpuscles, after treatment, was 3.1 mg. per 100 c.c., and this is 6 per cent below the control value.

#### Ester Phosphorus.

-c0o-

Whole Blood: The ester phosphorus of the whole blood, after treatment, was 16.35 mg. per 100 c.c., a decrease of 3.6 per cent below the control value.

Plasma: The ester phosphorus of the plasma, after treatment, was 0.6 mg. per 100 c.c., an increase of 100 per cent above the control value.

Red/

Red Blood Corpuscles: The ester phosphorus of the red blood corpuscles, after treatment, was 45.3 mg. per 100 c.c., an decrease of 10 per cent below the control value.

Lipin Phosphorus.

-oOo-

Whole Blood: The lipin phosphorus of the whole blood, after treatment, was 11.8 mg. per 100 c.c., or 3.2 per cent below the control value.

Plasma: The lipin phosphorus of the plasma, after treatment, was 8.7 mg. per 100 c.c., or 20.8 per cent above the control value.

Red Blood Corpuscles: The lipin phosphorus of the red blood corpuscles, after treatment, was 17.5 mg. per 100 c.c. or 21.1 per cent below the control value.

Total Phosphorus.

-oOo-

Whole Blood: The total phosphorus of the whole blood, after treatment, was 31.0 mg. per 100 c.c., i.e. 2.5 per cent below the control value.

Plasma: The total phosphorus of the whole blood, after treatment, was 12.0 mg. per 100 c.c., i.e. 22.4 per cent above the control value.

Red Blood Corpuscles: The total phosphorus content of the red blood corpuscles, after treatment, was 65.9 mg. per 100 c.c., representing 13 per cent below the control value.

Haematocrit Finding.

-c0o-

The cellular portion of the whole blood, after treatment, was 35.2 c.c. per 100 c.c., representing 5.7 per cent above the control value.

Summary.

-c0o-

1. The free phosphorus showed a tendency to rise in amount per 100 c.c. of the whole blood, and of the plasma, and to fall in amount per 100 c.c. of the red blood corpuscles after treatment.
2. The ester phosphorus showed a tendency to fall in amount per 100 c.c. of the whole blood, and of the red blood corpuscles, and to rise markedly in amount per 100 c.c. of the plasma after treatment.
3. The lipin phosphorus showed a tendency to diminish slightly per 100 c.c. of the whole blood, to diminish markedly per 100 c.c. of the red blood corpuscles, and to increase markedly per 100 c.c. of the plasma after treatment.
4. The total phosphorus content was slightly decreased in the whole blood, appreciably so in the red blood cells, and markedly increased in the plasma per 100 c.c. after treatment.
5. The cellular portion of the blood showed a tendency to increase in amount per 100 c.c. after treatment.

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General Discussion.

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Buckman, Daland, and Weld (1925) as mentioned above studied the blood phosphorus in chronic myelogenous leukaemia, especially as influenced by X-rays therapy. They found that a marked increase in the amount of the total phosphorus content not only of the plasma, but also of the red blood corpuscles generally occurred. Since, however, they determined only the total, and the inorganic phosphorus of the whole blood, of the plasma and of the red blood corpuscles per 100 c.c., they could not have appreciated the complete nature of the qualitative change in the phosphorus. They reported an increase in the amount of the total phosphorus both in the plasma, and the red blood corpuscles per cent. Our results, presented in this communication, for the plasma and the red blood corpuscles support their findings for the plasma, but not for the corpuscles. The total phosphorus content of the red blood cells in our cases, showed a tendency to diminish in amount per 100 c.c. after X-rays irradiation. The difference in amount per cent between their findings and ours might be due entirely to the fact that the disease for which they administered X-rays therapy was different to those studied by us.

From the available results there can be no doubt as to the effect produced upon the partition of the phosphorus compounds/



compounds of the blood by the administration of X-rays. These rays apparently must cause a certain reaction in the tissue of the body which markedly affects the distribution of the phosphorus compounds in the blood. These changes in the partition of the phosphorus compounds of the blood probably set in immediately after the administration of the X-rays therapy, for they are evident 24 hours after the irradiation, and they are still present in the blood at the end of 5 days after the treatment. It would probably have been of great importance to follow these changes and find out how long they persist, but the circumstances coupled with the large quantities of blood required for each analysis prevented the experiment.

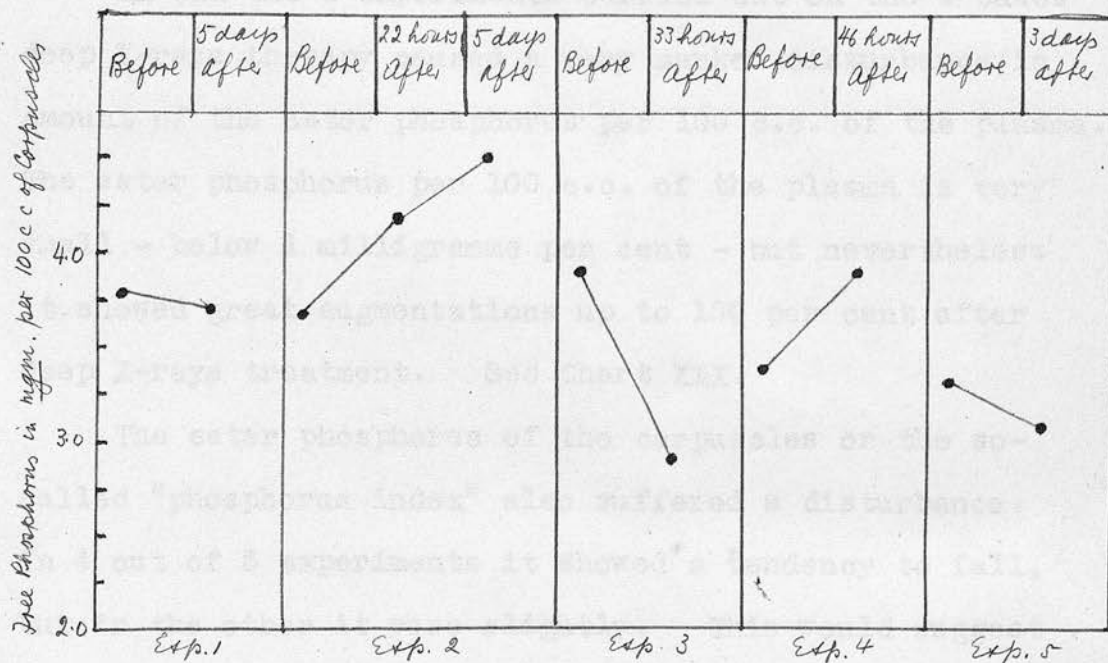
#### Free Phosphorus.

-oOo-

In 5 experiments carried out on 4 cases, there was found an appreciable increase or decrease in amount of the free phosphorus fraction per 100 c.c. of the plasma, and of the red blood corpuscles, but there was no uniformity in these changes. Thus, the free phosphorus of the plasma showed a tendency to fall in amount per cent in 3 experiments, to remain constant in one, and to increase in the remaining experiment. Similarly the free phosphorus of the corpuscles showed a tendency to fall in 3 experiments per cent, and in the other two to increase in the amount per cent. See Chart XVII and XVIII.

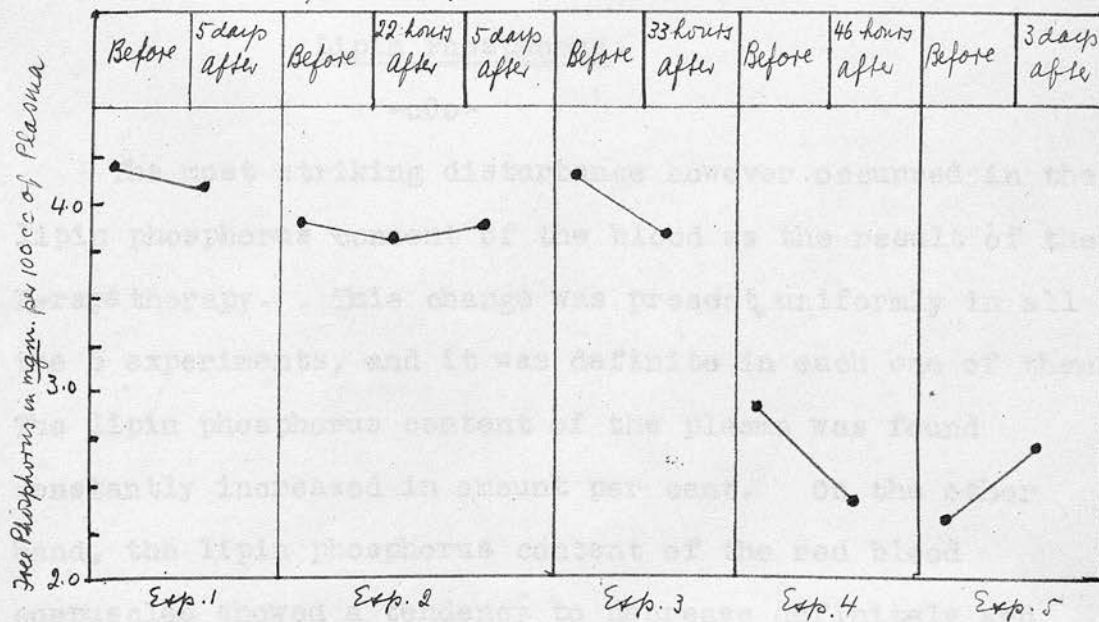
# Chart XVII

Showing the Effect of X-rays Therapy on the partition of Phosphorus compounds of Blood.



# Chart XVIII

Showing the Effect of X-rays Therapy on the Partition of Phosphorus compounds of Blood.



Ester Phosphorus.

-oOo-

In all the 5 experiments carried out on the 4 cases deep X-rays therapy caused a very marked disturbance in amount of the ester phosphorus per 100 c.c. of the plasma. The ester phosphorus per 100 c.c. of the plasma is very small - below 1 milligramme per cent - but nevertheless it showed great augmentations up to 100 per cent after deep X-rays treatment. See Chart XIX.

The ester phosphorus of the corpuscles or the so-called "phosphorus index" also suffered a disturbance. In 4 out of 5 experiments it showed a tendency to fall, but in the other it rose slightly. This would suggest that the corpuscles are poorer in the ester phosphorus per unit volume after treatment. See Chart XX..

Lipin Phosphorus.

-oOo-

The most striking disturbance however occurred in the lipin phosphorus content of the blood as the result of the X-rays therapy. This change was present uniformly in all the 5 experiments, and it was definite in each one of them. The lipin phosphorus content of the plasma was found constantly increased in amount per cent. On the other hand, the lipin phosphorus content of the red blood corpuscles showed a tendency to decrease definitely and constantly in amount per cent. This observation would strongly/

# Chart XIX.

The Effect of X-rays therapy on the Partition of Phosphorus Compounds of Blood.

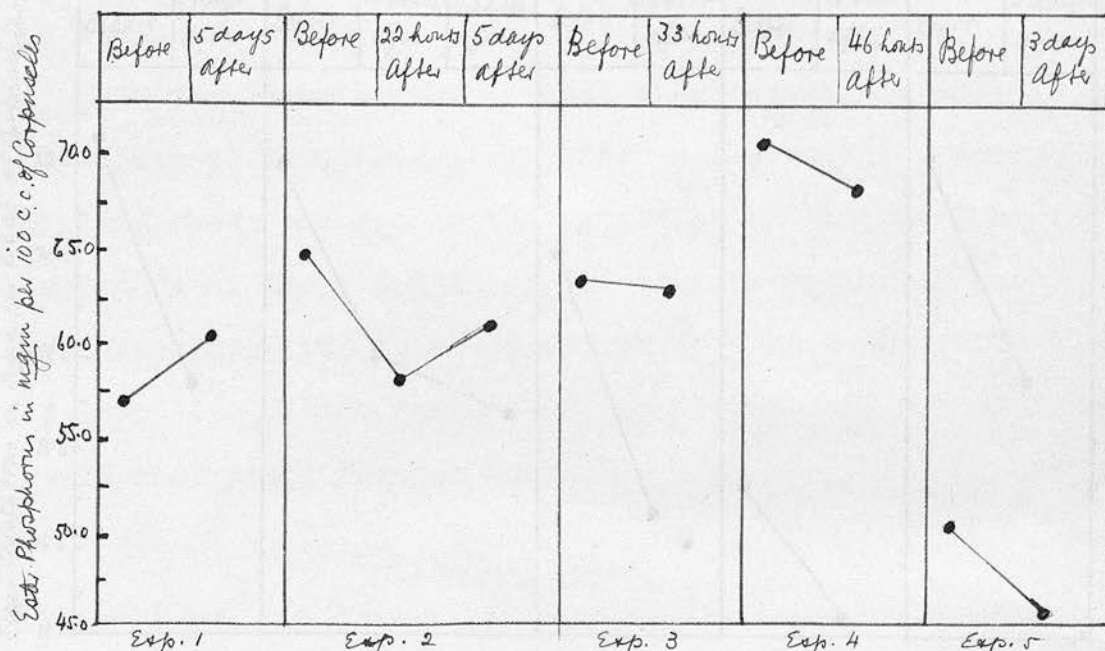


Chart XX - The Effect of X-ray Therapy on the Partition of Phosphorus Compounds of Blood.

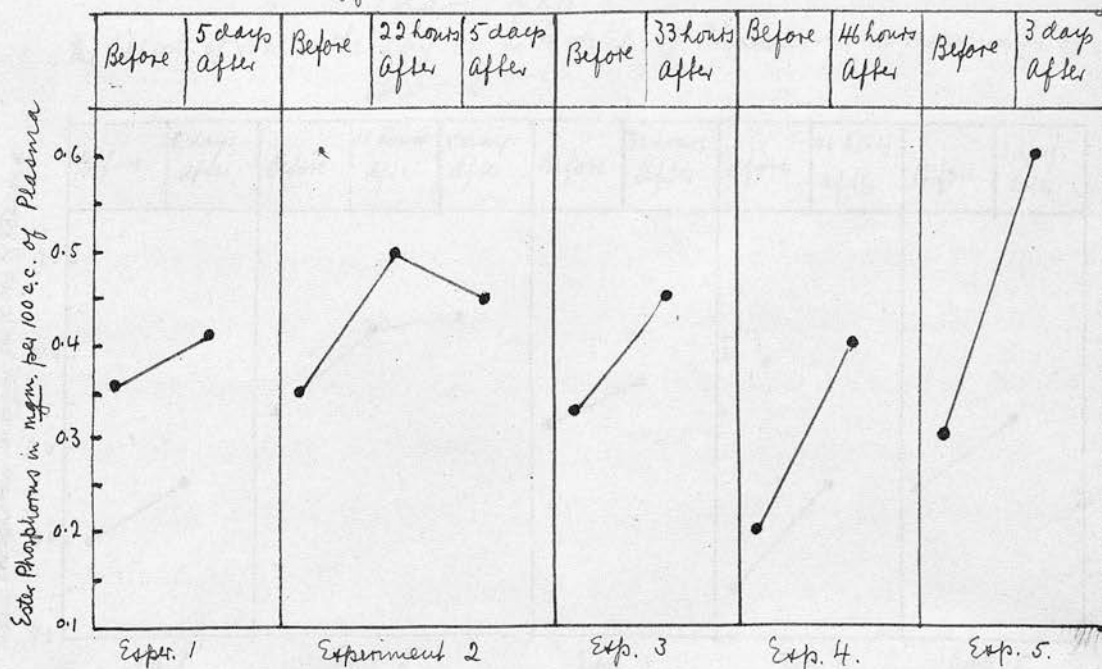




Chart XXI.

The Effect of X-rays Therapy on the Partition of Phosphorus Compounds of Blood.

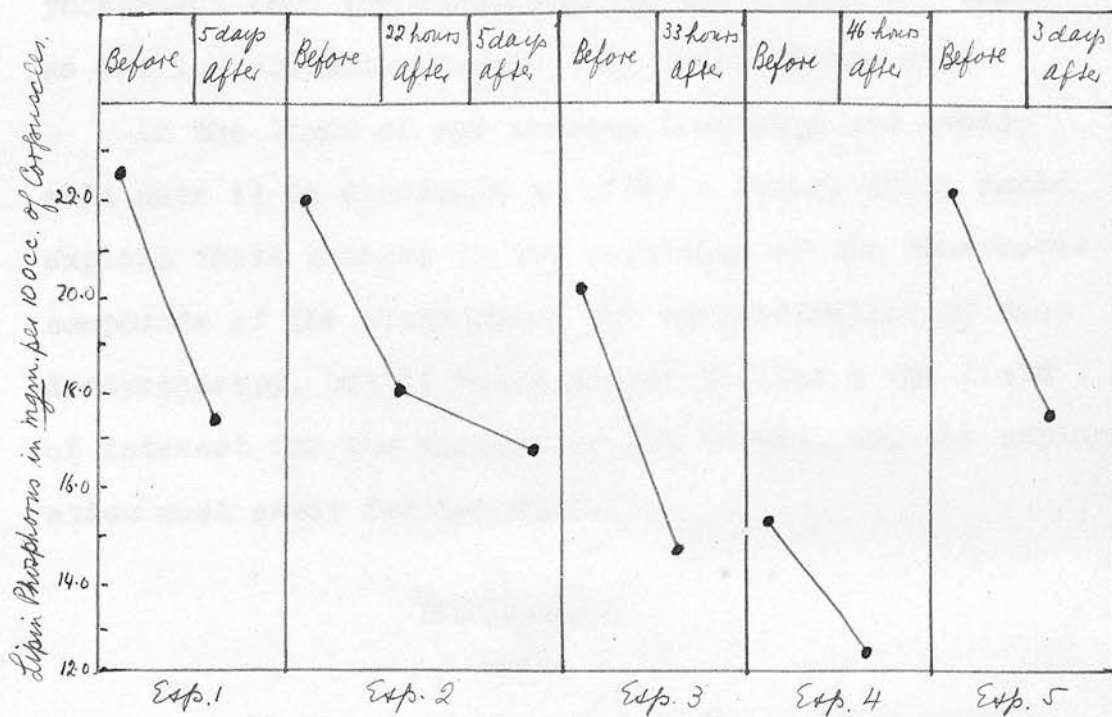
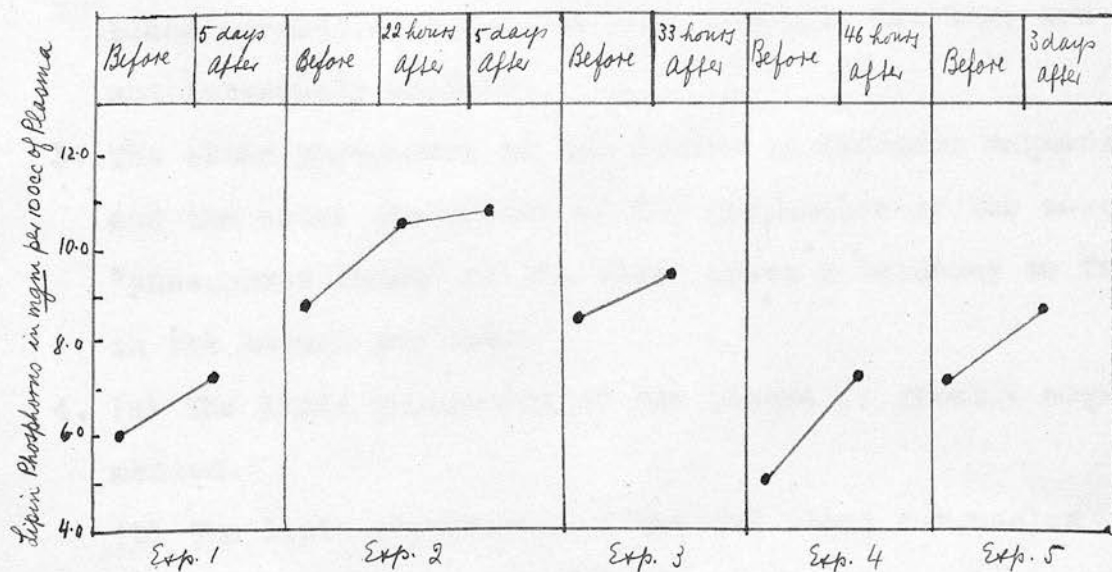


Chart XXII

The Effect of X-rays Therapy on the Partition of Phosphorus compounds of Blood.



strongly suggest that there is a shift of the lipin phosphorus from the corpuscles to the plasma for some as yet inexplicable reason. See Chart XXI and XXII.

In the light of our present knowledge and available data it is difficult to offer a theory which would explain these changes in the partition of the phosphorus compounds of the blood after the administration of deep X-rays therapy, but it would appear to open a new field of interest for the workers of the future, and the explanation must await further work.

#### Conclusions.

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1. The administration of X-rays therapy influences the partition of the phosphorus compounds of the blood.
2. The free phosphorus both of the plasma, and the red blood corpuscles undergoes some changes, but they are not invariably uniform.
3. The ester phosphorus of the plasma is markedly augmented, and the ester phosphorus of the corpuscles or the so-called "phosphorus index" of the blood shows a tendency to fall in the amount per cent.
4. (a) The lipin phosphorus of the plasma is greatly augmented.  
(b) The lipin phosphorus of the red blood corpuscles shows a tendency to be markedly decreased in the amount per cent.

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Appendix I.

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Case 1. J.McE., aet. 11 years. Admitted 1/12/1929.

History: Caught cold 3 weeks ago. Headache 2 weeks ago. Malaise, vomiting and swelling of face for 1 week. Blindness for 1 day.

On examination: big and fat boy, unconscious, will not speak. Slight oedema over shins. Vision cannot be tested. Optic neuritis in both eyes, most marked in the left eye. Throat clean. Circulatory, respiratory, alimentary and nervous systems - nil. Urine contains albumin ++, blood +. Blood pressure  $\frac{160}{130}$  N.P.N. 32.1 mg.%; Cl' 410 mg.%. Blood examined for phosphorus compounds. 3/12/1929 Condition I.S.Q. N.P.N. 54.5 mg.%; Cl' 270 mg.%. Blood examined for phosphorus compounds. 20/12/1929 Quite bright. Vision good. No neuritis. Urine contains albumin +, and abundant casts. Slight pitting still present over shins. N.P.N. 57.1 mg.%, Cl' 260 mg.%. Pigment test: 1st hour 27%, 2nd hour 13%. Urea concentration test: before 1.32%, 1st hour 2.27%, 2nd hour 2.10%. Blood examined for phosphorus compounds. 13/1/30 Urine contains no albumin. Few casts. Blood examined for phosphorus compounds. 20/1/30 Dismissed well.

Diagnosis: acute nephritis with uraemia.  
9/5/30 seen outdoors; general condition satisfactory. Urine clear. Blood examined for phosphorus compounds.

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Case 2. M.J., aet. 6 years. Admitted 18/2/1930.

History: Headache and vomiting for 3 weeks; swelling of face and legs for 2 weeks.

On examination: fair-sized, acutely ill and unconscious. Oedema of face, feet and ankles. Heart faint systolic murmur at pulmonic area. Lung: Some scattered rhonchi. Urine contains albumen +++, blood +, RBCs, WBCs, epithelial and granular casts. Blood pressure  $\frac{160}{105}$   $\frac{1}{2}$  Slight blurring of the discs especially of the right eye. N.P.N. 84.4 mg.%; Cl' 330 mg.%; CO<sub>2</sub> 46.9 vols.%. Blood examined for phosphorus compounds. 21/2/30. Condition I.S.Q. Blood examined for phosphorus compounds. 7/3/30. Urine contains albumin +, blood  $\pm$ ; Esbach 0.5. N.P.N. 34 mg.%; Cl' 290 mg.%. Urine concentration test: before 0.6%, 1st hour 1.38%, 2nd hour 1.8%. Blood examined for phosphorus compounds. 5/5/30. Urine contains a trace of albumin, Esbach nil, and occasional pus cell. Blood examined for phosphorus compounds. Dismissed well.

Diagnosis: acute nephritis with uraemia.

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Case 3. H.J., aet. 5 years. Admitted 13/1/1930.

History: Swelling of the feet, legs, hands and face of 5 days' duration. Haematuria for 3 days.

On examination: Well nourished with slight generalised oedema. Free fluid in abdomen. Teeth bad. Other organs nil. Urine contains albumin ++, blood +, RBCs and casts. Blood pressure  $\frac{132}{95}$  N.P.N. 39.7 mg.%; Cl' 310 mg.%. Blood examined for phosphorus compounds. 25/2/30. Urine contains albumin +, and few granular casts. Blood examined for phosphorus compounds. 12/3/30. All oedema gone. Urine contains albumin +, and occasional RBCs. Blood examined for phosphorus compounds. 27/3/30. Pigment test 45% in 2 hours. Urine contains a trace of albumin, and occasional casts. Urea concentration test: before 1.02%, 1st hour 2.73%, 2nd hour 3.10%. Blood examined for phosphorus compounds. 28/3/30. Dismissed well.

Diagnosis: acute nephritis.

25/4/30: seen outdoors: general condition good. Urine clear. Blood examined for phosphorus compounds.

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Case 4. G.S., aet. 6 years. Admitted 22/2/1930.

History: Fevered and urine brown for 10 days. Vomited once.

On examination: Tall spare boy. No oedema. Basal systolic murmur. Throat clean. Tonsils +, carious teeth. Urine contains albumin ++, blood ++, granular and cellular casts. 24/2/30. Blood pressure  $\frac{100}{60}$  N.P.N. 62.3 mg.%. Blood examined for phosphorus compounds. 24/3/30. Quite well. Urine contains a trace of albumin. Pigment test 62% in 2 hours. Urea concentration test: before 1.86%, 1st hour 2.76%, 2nd hour 3.12%. Blood examined. 31/3/30. Dismissed well.

Diagnosis: acute nephritis.

16/5/30: seen outdoors: general condition satisfactory. Urine clear. N.P.N. 44.4 mg.%. Blood examined.

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Case 5. E.McC., aet 9 years. Admitted 13/2/1930.

History: Puffiness of face for 1 week. Urine brown. Headaches in the morning for 3 days, and nausea. Anoxeia for 2 days. Bowels rather loose.

On examination: Well developed and nourished boy. Swelling of face and slight pitting round the ankles. Throat clean, carious teeth. Urine contains albumin ++, blood +, and epithelial and granular casts. Blood pressure  $\frac{160}{120}$ . 15/2/30. Urine contains albumin ++, blood +, Esbach 1.25. N.P.N. 43.5 mg.%; Cl' 300 mg.%. Blood/

Blood examined. 7/3/30. Urine contains albumin +, and few casts. N.P.N. 31.6 mg.%; Cl' 300 mg.%. Urea concentration test: before 1.2%, 1st hour 2.4%, 2nd hour 3.12%. Blood examined. 20/3/30. Dismissed well.

Diagnosis: acute nephritis.

12/5/30: seen outdoors: general condition good. Urine clear. Blood examined.

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Case 6. D.D., aet 8 years. Admitted 2/11/1929.

History: 6 days ago shivering and pain in right loin.

Urine dark. Off food and vomiting.

On examination: fair-sized and moderately nourished boy. Urine contains albumin ++, blood +, and RBCs and granular casts. Blood pressure.  $\frac{85}{60}$

Blood examined for phosphorus compounds.

Diagnosis: acute nephritis.

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Case 7. H.H., aet  $3\frac{1}{2}$  years. Admitted 19/4/30.

History: Haematuria for 3 weeks. Restless and easily tired. Appetite poor. Anuria for 2 days.

On examination: Small, fairly well nourished girl. No oedema. Systolic murmur all over precordium propagated towards left axilla. Throat congested.

Urine contains albumin ++, blood +, RBCs and casts.

N.P.N. 71.4 mg.%, Cl' 330 mg.%. Blood examination for phosphorus compounds. Dismissed well.

Diagnosis: acute nephritis.

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Case 8. H.M., aet 12 years. Admitted 21/3/30.

History: Headache and vomiting for 2 weeks. Puffiness of eyes.

On examination: Big spare boy. No oedema. All the organs normal. Tonsils ++. Urine contains albumin ++, blood +, granular casts. Blood pressure  $\frac{110}{60}$ . 4/4/30. Urine contains albumin ++, blood ++, Esbach 0.25, casts +. Blood examined for phosphorus compounds. 6/7/30. Dismissed well.

Diagnosis: acute nephritis.

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Case 9. J.W., aet 12 years. An outpatient. Urine contains slight trace of albumin. General condition good. Blood examination for phosphorus compounds.

Diagnosis: chronic nephritis.

(This patient was in the hospital one year ago).

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Case 10. A.McB., aet 11½ years. Admitted 31/1/30.

History: Swelling of feet and legs for 3 weeks. Puffiness of eyes for 1 week. Breathlessness for 1 day.

On examination: Undersized but well nourished.

Face cyanotic, clubbing of fingers and toes. Face puffy and oedema of feet, legs and lumbar region. Small cervical glands palpable. Lungs: impairment of note at both bases. Occasional rhonchi heard. Abdomen somewhat resistant. No tenderness. Throat red, carious teeth. Pirquet +. Urine contains albumin +++ and scanty granular casts. Blood examined. 22/5/30 Transferred to sanatorium.

Diagnosis: subacute nephritis and tuberculous peritonitis.

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Case 11. J.L., aet 5 years. Admitted 6/1/30.

History: Pale and listless for 7 weeks. Complained of thirst and frequent micturition. At the same time had special desire for sweet things. Albuminuria found. Measles 2 weeks later. Thirst became more marked.

Sugar in urine. Since then on diet + 10 units of insulin.

On examination: Big, moderately nourished boy. Pale. Cervical glands palpable. All the systems normal. Urine contains sugar and acetone. Fasting blood sugar 6.117%. Blood examined for phosphorus compounds on 3 occasions. 6/2/30 Dismissed on 1000 calories + 8 units of insulin.

Diagnosis: diabetes mellitus.

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Case 12. J.B., aet 10 years. Admitted 22/2/30.

History: Was treated in the hospital in 1928. Afterwards attended diabetic clinic every month. One month ago blood sugar was 0.3%. This was probably due to his adhering to the diet prescribed. Had cold 2 weeks ago.

On examination: Spare boy; not looking ill. Heart, lung, abdomen nil. Throat clean. Urine contains sugar +. Blood examined for phosphorus compounds on 3 occasions during his sojourn in the hospital.

7/4/30 Dismissed on diet of 1515 calories + 15 units of insulin.

Diagnosis: diabetes mellitus.



Case 13. J.McK., aet 8 years. Admitted 29/11/1929.

History: Was in the hospital in April 1929. Since dismissal attended diabetic clinic. Reported well with occasional glycosuria. Diarrhoea 1 week ago for 2 days. Abdominal pain. Fasting blood sugar 0.236% 3 days ago.

On examination: fair-sized, moderately well nourished girl. Cervical glands palpable. Circulatory, respiratory, alimentary and nervous systems nil. Throat clean. Tonsils +. Urine contains sugar ++ and a trace of acetone.

Blood examined for phosphorus compounds on 4 different occasions during her stay in the hospital. 5/5/30. Dismissed on diet of 1360 calories + 60 units of insulin.

Diagnosis: diabetes mellitus.

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Case 14. A.G., aet 10 years. Outpatient.

History: Was treated in the hospital in 1928, and has been attending diabetic clinic since. Is on a diet of 1320 calories + 24 units of insulin, and is doing well. Urine free of sugar, and fasting blood sugar 0.086%. Blood analysis for phosphorus compounds.

Diagnosis: diabetes mellitus.

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Case 15. J.K., aet 1 years. Admitted 23/12/1929.

History: at year crowing sounds on wakening out of sleep. Convulsion 10 days ago. Crowing still present.

On examination: fair-sized and moderately nourished infant. Looks well. Anterior fontanelle admits 1 finger tip. Beading of the ribs. Facial phenomenon present. X-ray of wrists showed slight rickets. Blood examination. 15/3/30 dismissed well after treatment with Vigantol.

Diagnosis: infantile tetany with rickets.

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Case 16. J.M., aet 4 years. Admitted 27/1/1930.

History: Healthy till 3 years old when had measles followed by pneumonia. Since then his legs have been weak. Unable to stand.

On examination: Markedly rachitic child with narrow chest and splaying of the central margin. Tibiae bowed and epiphyscal enlargement. Throat red, carious teeth. X-ray of wrists: rickets? healing. 5/2/30 Laryngismus and very marked facial phenomenon. Blood analysed for phosphorus compounds. 17/3/30 Dismissed improved.

Diagnosis: infantile tetany with rickets.

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Case 17. J.C., aet 1 years. Admitted 25/1/1930.

History: Attacks of respiratory embarrassment and "swelling of abdomen" for 2 months. Respiratory embarrassments are accompanied with crowing noise. Sweats profusely.

On examination: Fair-sized and moderately nourished. Irritable, and when crying tendency to laryngismus. Anterior fontanelle admits 1 finger tip. Beading of ribs, and epiphyseal enlargement. Facial phenomenon very marked. X-ray shows "slight rickets" ? healing. Blood examination. Put on vigantol.  
22/3/30 Dismissed well.

Diagnosis: infantile tetany with rickets.

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Case 18. T.M., aet years. Admitted 17/2/30.

History: Attacks of dyspnoea for 4 months. 2 convulsions during the past 2 weeks. Has inspiratory stidor, occasionally cyanosed during the attack.

On examination: Fair-sized and well nourished infant. Very pale with suggestion of cyanosis in cheeks. Breathing noisy. Typical laryngismus heard. Blood examined.  
20/2/30 died.

Diagnosis: infantile tetany.

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Case 19. G.T., aet 1 years. Admitted 23/3/30.

History: Crowing for 2 weeks. Vomited for 2 days. Spasm of hands and feet which comes and goes since.

On examination: Big well nourished girl. Irritable. Definite laryngismus. Carpo-pedal spasm present. Anterior fontanelle admits 2 finger tips. Beading of ribs and epiphysis enlarged. Facial phenomenon very marked.  
1/4/30 Dismissed well.

Diagnosis: infantile tetany with rickets.

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Case 20. J.L., aet 2 years. Admitted 7/2/30.

History: Spasm of hands and feet of few hours' duration.

On examination: Small spare child. Flushed. Anterior fontanelle admits 1 finger tip. Very marked carpo-pedal spasm. Beading of ribs and epiphysis enlarged. Facial phenomenon very marked. X-rays show "rickets!" Blood examined.  
21/2/30 Dismissed apparently well.

Diagnosis: infantile tetany with rickets.

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Case 21. B.R., aet 4 weeks. Admitted 18/1/30.

History: Convulsions for 3 weeks.

On examination: Small and moderately nourished infant. No loss of skin elasticity. Anterior fontanelle admits 4 finger tips. No bulging present, pulsating. No nuchal rigidity. No facial phenomenon. Urine nil. Lumbar puncture. C.S.Fluid clear. No increase in cells and Pandy negative. Wasserman Reaction (blood) negative. Blood examination for phosphorus compounds. 26/2/30 Died.

Diagnosis: idiopathic convulsions.

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Case 22. G.K., aet 5 weeks. Admitted 22/1/30.

History: Diarrhoea for 9 days. Convulsions for 3 days.

On examination: Small fairly well nourished infant. Anterior fontanelle admits 3 finger tips, and pulsating, facial phenomenon negative. Urine nil. No nuchal rigidity. Blood examination. 6/3/30 Dismissed apparently well.

Diagnosis: idiopathic convulsions.

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Case 23. R.A., aet 12 years. Admitted 23/12/29.

History: Listless and loss of appetite for the last few months. During the last 6 weeks he grew worse.

On examination: Small, rather spare boy, of pale and sallow complexion. Mucosae very pale. Cervical glands palpable. Circulatory, respiratory, alimentary and nervous systems nil. Tonsils +++. Some carious teeth. Urine is acid in reaction and contains a trace of acetone. Blood count: HC. 40%, RBCs 4,600,000, WBCs 3.100, C.I. .43. Wasserman reaction (blood) negative. Blood examined for phosphorus compounds. 4/2/30 Dismissed well.

Diagnosis: secondary anaemia.

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Case 24. L.A., aet 6 years. Admitted 3/4/1930.

History: The child has been disinclined to play and has been getting pale for past year.

On examination: Fairly well nourished. Marked palor of skin and mucous membranes. Small lymphatic glands palpable in the axillae and groins. Heart: systolic murmur loudest at base. Carious teeth. Urine nil. Blood count: HC. 20%, RBCs 2.500,000, WBCs 7.200, C.I. 0.4. Fragility test: negative. Wasserman Reaction (blood) negative. 16/5/30 Dismissed much improved.

Diagnosis: secondary anaemia.

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Case 25. D.S., aet 8 years.

This patient had rheumatic fever, and was in convalescent stage, but was very anaemic. Blood count: HB. 35%, RBCs 4.700,000; WBCs 7.400; C.I. .37. Blood examined.

Diagnosis: secondary anaemia post rheumatic fever.

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Case 26. M.T., aet 3 years. Admitted 30/1/30.

History: Bruises appeared on legs, side of face and back.

On examination: Big, good coloured healthy looking boy with bruises over legs, right hand, face and back. Petechial haemorrhages over shoulders and buttocks.

Heart: systolic murmur at base. Tonsils +. Urine nil.

Blood examined. 5/2/30 Dismissed well.

Diagnosis: purpura simplex.

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Case 27. W.M., aet 6½ years. Admitted 25/11/1929.

History: Child born with "fracture of the left tibia". Was operated on aet ½ years at R.H.S.C., and since has been walking with the aid of a high boot. Attended outpatient department regularly till present.

On examination: Acute bowing in the lower third of left tibia with a small ulcerating area at the apex of the bowing. Fracture exposed and bones plated, but no union ensued. Wasserman Reaction (blood) negative.

Diagnosis: ununited fracture of tibia.

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Case 28. J.W., aet 1 years. Admitted 11/2/1930.

History: As she has not made any attempt to walk mother brought her to R.H.S.C.

On examination: Small, well nourished child; has dull and heavy look. Keeps mouth open. Anterior fontanelle admits 1 finger tip. Beading of ribs. Epiphysis enlarged. Cervical glands palpable. Urine nil. X-ray shows rickets. ? active.

Diagnosis: rickets.

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Case 29. D.M., aet 5½ years. Admitted 24/3/30.

History: Urine contains albumin.

On examination: Fair-sized and well nourished girl. No puffiness or swelling anywhere. Urine contains albumin/



albumin if the patient passes it in standing posture, and none when at rest.

Diagnosis: functional or orthostatic albuminuria.

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Case 30. H.M., aet 8 years. Admitted 5/4/1930.

Palor for a few months and enlarged glands in the neck.

On examination: Big boy, and not acutely ill. In posterior triangle on the right side of the neck large masses of discrete glands. No glands anywhere else. Spleen not palpable. A gland excised and examined. Pathological report: Histologically gland is the seat of lymphadenoma.

Diagnosis: lymphadenoma.

This patient was treated with X-rays, and used for the experiment.

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Case 31. C.G., aet  $9\frac{1}{2}$  years. Admitted 30/1/1930.

History: Mother has noticed that she has not been growing at all since 5 years old. Periodical attacks of vomiting and diarrhoea.

On examination: Small and plump girl. Quite bright. All the systems nil. Throat clean. Urine nil. Height 102.5. Weight 16.92 kilos. X-ray of skull shows no abnormality. Her field of vision is within normal limits. Ossification centre practically normal. Goetsch's test was within normal limits. Blood examined. Put on to pituitary extract twice weekly for 2 months. Blood re-examined.

Diagnosis: ? Pituitary dwarfism.

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Case 32. C.M., aet 7 years. Diagnosis: haemangioma of thigh.

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Case 33. E.McA., aet 60 years.

Diagnosis: Carcinoma of the right mamma.  
Treated with deep X-ray therapy.

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Case 34. J.B., aet 33 years.

Diagnosis: cerebral cyst.  
Treated with deep X-rays therapy.

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